BUREAU OF HYGIENE AND TROPICAL DISEASES

BULLETIN OF HYGIENE

Volume 35, No. 1 January, 1960

The order of the contents of the *Bulletin of Hygiene* has been changed. The large section on Communicable Diseases has been placed farther back, next to the section on Bacteriology and Immunity, so that the papers relating to infections are grouped together; nevertheless, the two sections, though contiguous, are not combined. For convenience, however, papers on mycoses and mycology have been placed in a separate section.

Several sections formerly included have been abandoned, and some new sections have been created, in keeping with modern trends of public health interest.

The editors believe that this new arrangement will be more convenient to readers than the old arrangement. The schedule is as follows:—

PUBLIC HEALTH

General
Vital Statistics
Epidemiology
Maternal and Child Health
Health of Students, Nurses and Hospital Staffs
Health of Old Persons and the Chronically Ill
Chronic Cardio-Respiratory Diseases
Chronic Rheumatism
Cancer
Miscellaneous Diseases
Dental Health
Mental Health

SANITATION

General
Water and Swimming Baths
Sewage, Trade Waste and Refuse Disposal
Housing
Atmospheric Pollution
Port, Ship and Aviation Hygiene
Infestation

OCCUPATIONAL HYGIENE

General
Occupational Physiology
Occupational Diseases
Occupational Psychology
Heating, Lighting and Ventilation

FOOD AND NUTRITION

General
Foodstuffs
Food Poisoning

MYCOSES AND MYCOLOGY

COMMUNICABLE DISEASES

Tuberculosis
Venereal Diseases
General Infective Diseases
  General
  Hospital and Other Cross Infections
General Infective Diseases—*cont.*
  Coccal Infections
  Bacterial Infections
  Virus Infections
Other Communicable Diseases

BACTERIOLOGY AND IMMUNITY

General
Bacteriostatic and Bactericidal Substances; Disinfection
Bacteria
Rickettsiae
Bacteriophages
Viruses
Immunity

MISCELLANEOUS

BOOK REVIEWS

Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

MINISTRY OF HEALTH. **Report of the Ministry of Health for the Year ended 31st December, 1958. Part I. 1. The National Health Service (including a Chapter on International Health). 2. Welfare, Food and Drugs, Civil Defence.** Cmnd. 806. pp. xxv+365. 1959. London: H.M. Stationery Office. [15s. 6d.]

This informative annual report contains 111 pages more than its predecessor [this *Bulletin*, 1959, v. 34, 305]. The increase in size is accounted for by each section giving a survey of the main developments since the National Health Service started in July 1948. This enhances greatly the value of the report which is, in fact, a 10-year history. In his foreword the Minister deals in a statesmanlike way with the numerous questions of high policy which have arisen during the 10 years.

Finance. The total gross cost of the National Health Service in the financial year 1957–8 was £626m. which is £41m. more than in the previous year. The sources of the money during 1948–58 were: the Exchequer, 78% (75·7%); the National Insurance Fund, 7·9% (8·9%); patients' contributions, 3·7% (1·0%); local authorities' rates 4·0% (3·5%) and superannuation contributions and transfer values, 5·3% (5·2%): the figures in brackets are those for 1949–50. An Act to increase insurance contributions has just been passed and it is estimated that in the financial year 1958–9 the Exchequer contribution will fall to 72·4% and that from the Insurance Fund will rise to 13·8%.

A table shows the rise in cost year by year since 1954–5. It is estimated that 70% of the increase since the service began has been due to "inflationary trends in the economy" and their effect on prices and staff remuneration.

A break-down of the gross costs for 1957–8 shows that hospital running costs accounted for £337,587,632; capital expenditure on hospitals, £17,819,995; general medical services, £62,800,775; pharmaceutical services, £53,319,704; general dental services, £34,459,453 and supplementary ophthalmic services, £8,903,187. The 50% grant for local authority services amounted to £26,449,655.

Hospitals. The number of beds available was 477,000: this is 6% more than in 1949 but the patients treated in them increased by 30%. A new table gives the allocation of beds to departments for each of the past 10 years: beds for the acute infectious diseases have gone down from 4·6 to 1·7% and for diseases of the chest from 6·0 to 5·1%. Increases include chronic sick and geriatrics from 11·5 to 12·0% and mental disorder from 41·8 to 44·3%. Surgical departments now occupy 14·8% of the beds compared with 12·1% in 1949. Patients waiting for a medical bed are 44% fewer than 10 years ago and for a surgical bed 10% fewer but for surgery the figure has risen by 23% if ear, nose and throat beds are excluded.

There has been a welcome increase in the amount of money available for hospital building.

The psychiatric services are receiving close attention: there is a revolt against long-term confinement in hospital: there are now 35 "day" hospitals and there were over a million attendances at psychiatric out-patient clinics: the average number of beds available in mental hospitals during 1958 was 151,720 compared with 154,805 in 1957.

The tuberculosis figures are encouraging. In the 10 years the annual number of deaths has declined from 21,993 to 4,480, and the number of occupied beds from 26,115 to 17,429.

There are valuable sections on artificial limbs, hearing aids, the National Blood Transfusion Service, Hospital Supplies, medical rehabilitation, hospital pharmacy, radio-active substances and the Hospital Organization and Methods Service.

The number of domiciliary visits by consultants has more than doubled in the 10 years and is running at nearly 300,000 a year.

There has been a further increase (86) during 1958 in the number of consultants which is now 6,988. There are 4,654 more whole-time nurses making 143,331 and 179 more midwives making 9,178.

Domiciliary Services. The number of doctors providing general medical services increased during the year by 144 making 20,439 and the average number of patients on a doctors' list is 2,267. The distribution is better and the proportion of the population living in areas served by too few doctors has gone down from 51·5% in 1952 to 18·6%.

There are 10,274 dentists engaged in the service and last year they dealt with over 12 million patients. There was a welcome increase in conservative treatment, and the number of dentures supplied, 3 million in 1950, fell to 1,300,000 in 1958. The demand for orthodontic treatment is increasing.

There was a slight decline to 203,384,933 in the number of prescriptions dispensed but a rise in the average cost which is now 77·26d. per prescription. Proprietary preparations account for 75% of the total cost.

The number of domiciliary confinements attended by midwives in 1958 was 265,215, an increase of 9,468 over the previous year: a doctor was present at the delivery of 44,964 of them. There was a slight increase

in the attendances at local authority ante-natal clinics and a more substantial one at their child welfare clinics. Public day-nurseries are being closed and now number only 501 compared with 1,535 in 1944 but private nurseries and registered child minders are increasing and now number 544 and 1,138 respectively.

The home nursing service employs 10,189 nurses who paid 24,372,849 visits, a small reduction on the previous year.

The domestic help service continues to expand and in 1958 271,968 families were helped: some authorities use this service for the rehabilitation of problem families.

The total number, including part-time, of Health and Tuberculosis Visitors was 6,885 who paid over 11 million visits.

There is a long section on local authority mental health services. There has been much activity in the provision of occupational centres for the mentally defective.

The wisdom of the abandonment of so-called compulsory vaccination against smallpox and its replacement by an intensive campaign for free voluntary vaccination is slowly being justified: the average vaccination rate for infants was 36·8% in 1937–46: in 1958 it was 44·5.

The great and pervading importance of health education is stressed. A few new health centres were opened during the year. The most expensive service provided by the local authorities is the ambulance service.

There are valuable chapters on the central supply and pricing of goods required by the National Health Service, and also on the steps taken to regulate the pay of those employed in the service.

The Welfare section deals mainly with the care of the aged. In the 10 years since 1948 the number of persons in the population aged 75 or more has increased by 406,000 to 1,887,000. There is an enlightened section on the improvements made in residential accommodation for the aged. At the end of 1958 there were 79,877 persons, mostly aged, in residential welfare homes and 4,746 in temporary accommodation.

There are 96,475 names on the register of the blind and the registers of other handicapped persons are being built up.

There are 95 pages of statistics in the appendices and 117 statistical tables in the text.

This review has been almost an abstract as in order to reveal the scope of the report many figures have had to be included but, even so, they are only a minute fraction of the total amount of information included in this encyclopaedic volume.

The fun of looking for discrepancies in the text or among the figures has been unrewarding.

The report is essential reading and a handy work of reference for all concerned in any branch of the National Health Service and will be of great value to foreigners who wish to learn about how this great and unique social experiment is progressing.

Allen Daley

WAR OFFICE. **Report on the Health of the Army 1955.** pp. iii+127, 4 figs. & 7 charts. 1959, July 3. London: War Office [W.O. Code No. 12369; 24/General/3960].

The Annual Report on the Health of the Army for 1955 is presented in the same form as in previous years [for 1954 report, see this *Bulletin*, 1958, v. 33, 721]. The subject-matter is in 8 chapters entitled the recruit, the army health organization and its work, medicine and allied specialities, surgery: including allied specialities, pathology, the soldier's family, research and a statistical section. The statistical section which takes up about three-quarters of the report is in 16 parts and contains 35 tables of data.

The information contained in this report is set out clearly and succinctly and gives an excellent picture of the activities of the medical service of a modern army, whose forces are on duty in many different parts of the world. The health of the army in 1955 was well maintained although morbidity rates of certain diseases varied in different commands because of special conditions and country of service as, for example, the high incidence of leptospirosis in the Far East Land Forces in Malaya where in 1954 the rate per 1,000 effectives in the British Army reached a post-war maximum of 4·72. There are some interesting comparisons of hospital admissions in the period 1901–1955—in 1901 the total per 1,000 strength was 878·6 and in 1955 it was 205·5. Annual rates for certain diseases are recorded: enteric fever 5·9 in 1901 and 0·2 in 1955, malaria 119·1 in 1901 and 1·3 in 1955 and tuberculosis 4·4 in 1901 and 0·7 in 1955. The rate of fresh cases of venereal disease per 1,000 whether admitted to hospital or not has been reduced from 133·7 (1901) to 12·8 (1955). There has, however, been a considerable increase in the invalidings rate for psychiatric conditions from 1·4 (1901) to 4·6 (1955) although the latter is much less than the maximum of 10·5 reached in 1949. *M. E. Delafield*

STEWART, A. B. **London County Council Health Services.** *J. Roy. Inst. Pub. Health & Hyg.* 1959, Feb., v. 22, No. 2, 39–46.

This "outline description" of the London County Council's health services is written by the Council's Deputy M.O.H.

It begins by describing what the administrative County is and how it has developed from the Metropolitan Board of Works established in 1855. There are many "Londons" such as the City, Transport London, Police London, and Post Office London. The population of the County is being reduced as a deliberate policy and new towns are being developed to house those who are willing to move from the county area. Despite efforts to induce commerce and industry to go elsewhere it is estimated that more than 2 million people who work in London live outside it. (The present population of the administrative County is 3,254,000: in 1901 it was 4,536,500: the population of "Greater London" is 8,346,137.)

In 1891 London received its own Public Health Act

and in 1898 the Metropolitan Boroughs, with their quota of public health duties and powers, were formed.

The County is responsible for main drainage and 33,000 samples of Thames water and sewage in various stages of treatment are analysed yearly. The L.C.C. is unique among counties in being a housing authority (concurrently with the metropolitan boroughs), and the steps taken to adjudicate on medical certificates in support of rehousing are described.

The calls on the services of the county midwives are decreasing and 80% of the confinements in London occur in hospitals; but 40% of the expectant mothers of London attend the Council's ante-natal clinics.

There is a balanced section on health education and mention is made of day nurseries, infant welfare clinics, home nursing, health visitors, domestic helps and problem families. There is a tilt at a recent television programme where, it is alleged, the role of the local authority clinics was misrepresented.

There are good accounts of services given by mental health workers and of the work of the ambulance service. *Allen Daley*

AMIN, H. & ZAGLOUL, H. F. **The Present Status and Programme of Environmental Sanitation in Egypt.** *J. Egyptian Pub. Health Ass.* 1959, v. 34, No. 1, 1–35.

This paper describes the organization and functioning of public health services in Egypt, paying particular attention to environmental sanitation. The crude death rate of Egypt has been declining in all age groups since 1930 and this is attributed to decreased transmission of communicable disease. In 1938 a Department of Preventive Medicine was established in the Ministry of Health, consisting of 3 sections dealing respectively with control in respect of food, frontier and epidemics. The criticism is made that no single government unit is responsible for environmental sanitation.

Smallpox and louse-borne diseases are controlled by treating the population with insecticide twice yearly and vaccinating them every 4 years. Food-handlers and itinerant vendors do not receive a licence until proved free of communicable disease. Public companies or municipalities supply potable water to 6,700,000 people in the cities and around the Suez Canal. The rural population is served largely by pumps and wells. Some large schemes for supplying a further 5 million people are now being undertaken. The inhabitants of 15 towns have a sewerage system and 3 further sewerage schemes are under construction. The dried sludge is used as a fertilizer, and the effluent is disposed of by irrigation. A variety of types of latrine is employed in the rural areas and the tendency is to use night-soil to produce fertilizer. A country-wide sanitation programme has now been prepared. Refuse disposal is usually by tipping, but in Cairo some 200 tons daily are converted into fertilizer by an industrial plant. Control of vectors, comprising insects, snails and rats, is in charge of a special section. Docks and premises in port areas are dusted with insecticide twice a year. Schistosomiasis control is largely by snail destruction; in one area of 20 square kilometres vector snails have been eradicated by sodium pentachlorophenate. Nearly 15 million people live in malarious regions, where the disease is being controlled by larval control and residual spraying. A plan for complete eradication has been prepared, and it is thought this could be achieved in 5 years at a cost of £E.3 million above the annual expenditure of £E.600,000 on malaria.

Health education is successfully carried on by locally produced films and by the broadcasting of popular plays; models, specimens and illustrated literature are also used. *T. H. Davey*

FERREIRA, A. P. & GÂNDARA, A. F. Breves considerações sobre a província de Macau—seu aspecto sanitário. **[Sanitary Conditions in Macao]** *Anais Inst. Med. Trop.* Lisbon. 1958, Dec., v. 15, No. 4, 879–908, 1 map. [10 refs.] English summary.

VITAL STATISTICS

MARTINEZ, P. D., ALVAREZ ALVA, P., AVILA CISNEROS, I. & BRAVO BECHERELLE, M. A. Mortalidad de la niñez en México. **[Infant and Child Mortality in Mexico]** *Bol. Oficina Sanitaria Panamericana.* 1959, Aug., v. 47, No. 2, 101–17, 4 figs. English summary.

Between 1930, when vital statistics in Mexico became reliable, and 1956 the rate of infantile mortality has declined to a half (138 per 1,000 to 71); at ages 1–4 to a third (50 to 17); and at 5–14 years to less than a third (8·6 to 2·5).

Tables give a breakdown of the infant mortality in 1931–5 (134) and in 1951–5 (89·2) into the 10 principal causes. For both periods gastro-enteritis heads the list with a rate of 31·2 per 1,000 live births in 1931–5 and 18·6 in 1951–5: influenza and pneumonia as a combined heading come second with rates of 25·8 and 18·0 in the 2 periods. They are followed, but in different order in the 2 tables, by diseases peculiar to early infancy, such as prematurity, infections of the newly-born, asphyxia and atelectasis, and by infections such as bronchitis, whooping cough, malaria and tetanus which together with congenital malformations, dysentery, syphilis and measles complete the list of the 10 major causes of death taking the 2 periods together. In the 20 years deaths from infections have declined to about half but diseases peculiar to early infancy and congenital malformations show little change. Even in the later period gastro-enteritis and influenza and pneumonia caused 41% of the total mortality. Malnutrition is an important contributory factor in many of the deaths.

At ages 1–4 gastro-enteritis and influenza and pneumonia still head the list in each period followed in 1931–5 by whooping cough, malaria, measles, smallpox, bronchitis, typhoid fever, meningitis and diphtheria; but in 1951–5 smallpox, meningitis and diphtheria have gone from the first 10 and been replaced by accidents, dysentery and tuberculosis. In this age group the total mortality in 1931–5 was 48·4 per 1,000 and 26·2 in 1951–5.

At ages 5 to 14 the total mortality in the 20 years has been reduced from 7·5 to 3·3 per 1,000. Gastro-enteritis still heads both lists. Malaria is second in 1931–5 and third in 1951–5: influenza and pneumonia moved up from third in 1931–5 to second in 1951–5: in the fourth place there is smallpox in the earlier and accidents in the later period: measles, whooping cough, dysentery, typhoid fever, bronchitis and tuberculosis make up the rest in 1931–5: in 1951–5 heart disease appears and smallpox disappears.

A table gives the mortality rates at ages 1–4 for a number of other countries and another analyses the causes for Mexico, which has the highest rate (29·8), and for Sweden, which has the lowest (1·2). In Mexico 75% of the mortality is the result of infection.

Further analyses are made of the mortality in different parts of Mexico. They show that mortality is high where socio-economic levels are low as measured by meat consumption, illiteracy, housing standards and poverty.

Malnutrition is regarded as the most important factor producing the high infant and child mortality and this acts through a high incidence and case-mortality of the various infections. *Allen Daley*

MATERNAL AND CHILD HEALTH

LOWE, C. R. **Effect of Mothers' Smoking Habits on Birth Weight of their Children.** *Brit. Med. J.* 1959, Oct. 10, 673–6, 2 figs. [15 refs.]

The data of this enquiry were the records obtained from 2,042 women delivered in 6 Birmingham hospitals. The analysis has been mainly confined to the non-smokers (1,155) and regular smokers (668). On the average the non-smokers had the heavier babies, 7·33 lb., compared with 6·93 lb. for the babies of regular smokers. The mean weight of the infants of the heavy smokers (10 or more cigarettes a day) was slightly less than that of the light smokers (fewer than 10 cigarettes a day). The average weight of the male infants of the regular smokers was less than the average weight of the female infants of the non-smokers. The reduction in weight was greater among female infants than among male. Compared with those of the non-smokers the male infants of the light smokers were 0·25 lb. and the male infants of the heavy smokers 0·38 lb lighter and the female infants were 0·49 lb. and 0·56 lb., respectively, below the average of the female infants of the non-smokers. The period of gestation was similar in both the smoking and non-smoking groups. The weight of the non-smoking mothers before pregnancy was slightly but significantly greater than that of the mothers who smoked, but a comparison showed that for each group of mothers of similar weight the infants of the non-smoking mothers were the heaviest. The percentage of mothers who smoked regularly increased with parity in each age group of mothers but for both primiparae and multiparae the infants of the smokers were lighter than those of the non-smokers. The non-smokers had an insignificantly larger percentage of forceps deliveries (6·8) than the smokers (5·1). The percentage of pregnancies in which labour was surgically induced was significantly larger in the non-smokers (20·3) than in the regular smokers (15·0). The regular smokers had a slightly larger percentage of pregnancies without complications (83·2) than the non-smokers (80·4). The largest difference in the complications of pregnancy was that of toxaemia for which the non-smokers had 5·8 and the smokers 3·3 per cent.

The author concludes that smoking substantially reduces foetal growth. *W. J. Martin*

BOTHWELL, P. W. **The Epidemiology of Cigarette Smoking in Rural School Children.** *Med. Officer.* 1959, Sept. 11, v. 102, No. 11, 125–32, 7 figs. [18 refs.]

Data about the smoking habits and the conditions under which they were formed were obtained from 8,314 rural school children by means of a questionnaire. The proportion of boys who regularly smoked 1 cigarette a week ran from 16% at age 11 years to 39% at age 15 years; among girls the corresponding proportions were 2% and 16%. Boys who smoked, smoked more than girls; at age 15 years boy smokers smoked, on average, 18 cigarettes a week, while on average girls smoked only 6 cigarettes a week. Comparison with data collected for an industrial county borough shows that rural children smoked substantially less than town children.

Over half the boy smokers stated that they obtained their cigarettes from shops or slot machines. Among girls the commonest source of supply was "friends". Cinemas provided the commonest place for smoking (33% of places referred to by boys and 35% of those referred to by girls), but home was referred to only slightly less frequently. Approximately half the children said that their parents were aware that they smoked.

The mother's habits seemed to be the most important home influence. The probability of the child's smoking was about equal when the father smoked and when neither parent smoked, but it was about 50% greater when either the mother alone smoked or when both parents smoked.

The reasons most commonly given for starting smoking were curiosity, being given a cigarette and (to a less extent) a desire to be like others. Awareness of an association with ill health was common, and was commoner among non-smokers than smokers (81% against 61%). *Richard Doll*

FREEBAIRN, C. & SCOTT, G. A. **A Foot Survey of Stirlingshire School Children.** With a conclusion by E. N. REID. *Med. Officer.* 1959, Sept. 25, 155–60, 1 fig.

In September 1956 a chiropody service for all persons of pensionable age was begun in Stirlingshire on the decision of the Health Committee of the County Council. It was then agreed to investigate the manner of development of foot defects and their possible prevention and accordingly a survey of the feet of school children has been carried out which is described in this paper. The total of children examined was 1,024, made up of 128 children of each sex in the age groups of those born in 1952, 1948, 1944 and 1941. The selection of the children and the methods of examination used are described. An attempt was made to define precise standards of normality and these are stated under the headings:—(1) epidermophytosis, (2) hallux valgus, (3) pronation, (4) bad hygiene, (5) genu valgus and (6) unsatisfactory shoes which included Wellington boots worn on a dry day, casual shoes, canvas shoes, high heels (over $1\frac{1}{2}$ inches), footwear in very bad repair and footwear over one size too small. The findings of the investigation are described in considerable detail with tabulated data. Among the results recorded are:—(1) foot defects were found in 52% of all girls but in those born in 1941 the incidence was 80%; in boys the aggregate percentage was 37%; (2) in the oldest age group corns were present in 34·3% of girls and 10·1% of boys, hallux valgus in 54·6% of girls and 14·8% of boys and pronation in 25% of girls and 3·9% of boys. Unsatisfactory footwear was found in 62% of the girls (88% in those born in 1941) and in 30% of boys. The commonest defect in footwear was that it was too small. It was found, however, that there is no simple correlation between foot defects and unsatisfactory footwear.

"The need exists for a Foot Health Service for school children." *M. E. Delafield*

HEALTH BULL. Melbourne. 1957, Jan.–June, No. 117, 4–6, 1 fig. **Accidental Poisoning in Children.** [Extracted from an article by Jean ALLAN & H. WILLIAMS.]

This study was undertaken by the Clinical Research Department of the Royal Children's Hospital, Melbourne, during a 48-week period in 1954–55, in which 419 children attended the hospital for treatment of accidental poisoning. Investigations were carried out by a social worker into the circumstances of the accidents and the social background of 155 of these patients selected at random.

The results of the survey are stated shortly. Of the 419 cases, 332 were in children under the age of 3 years. These 419 children took 152 different types of poison grouped into:—(a) medicaments which included many of the commoner drugs found in most homes (193 children), (b) substances in common household use (174 children, of whom 97 swallowed petroleum products, 44 took turpentine and others furniture polish) and (c) miscellaneous including pest-control poisons, garden sprays and paints.

Of the 155 homes visited 63% were of good standard. The greater number of the children were of social class grouped as professional and business, and skilled tradesmen. Over three-quarters of the mothers were classed as average or good and the majority of the children appeared to be intelligent.

The main conclusion is that parents should be educated to realize the dangerous consequences of leaving poisonous materials within reach of the young child.

M. E. Delafield

MUKHERJI, P. S. & SUR, A. M. **Kerosene Poisoning in Childhood.** *Indian J. Child Health.* 1959, Aug., v. 8, No. 8, 430–37. [20 refs.]

Kerosene, used extensively in Indian households for lighting and cooking, particularly in poor homes, is one of the most common causes of accidental poisoning in India. In the period 1954–58, 80 children suffering from accidental poisoning were admitted to the paediatric unit of the Medical College Hospital, Nagpur, and in 33 of these the poison was kerosene. The case records of 27 of these 33 children were available and their analysis showed that:—(1) 22 children were in the age group 0–2 years, (2) 23 were male and 4 female and (3) 22 came from poor homes (monthly income less than 100 rupees).

There are some case reports and a clinical account of the main symptoms and signs which related to the gastro-intestinal, respiratory and nervous systems. More than half the patients were well by the end of 48 hours, the average stay in hospital was about 3 days but 2 children died of "depression" of the central nervous system. Treatment in 23 of the patients was by gastric lavage and the administration of parenteral penicillin. Poisoning by kerosene, its characters and treatment, are discussed with reference to much of the literature.

M. E. Delafield

FOLL, C. V. **An Account of some of the Beliefs and Superstitions about Pregnancy, Parturition and Infant Health in Burma.** *J. Trop. Pediatrics.* London. 1959, Sept., v. 5, No. 2, 51–9. [15 refs.]

CHRONIC CARDIO-RESPIRATORY DISEASES

ELLISON, Lois T., GALLAHER, B. S., LAMOTTE, Irene F., HAMILTON, W. F., Jr., ELLISON, R. G. & HAMILTON, W. F. **Clinical and Physiologic Results following Radioactive Iodine (I^{131}) in the Treatment of Chronic Pulmonary Insufficiency.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 181–7, 1 fig. [14 refs.]

The unsatisfactory results of treatment of severe pulmonary insufficiency are well known. It is reasonable to think that reduction of the metabolic requirements of the body might lead to symptomatic improvement. A preliminary trial showed that promising results were obtained by inducing hypothyroidism with radio-active iodine and a trial on 23 patients was started in June 1954. Full initial studies were carried out, of which details are given, and on their completion 25 mc. of radio-active iodine (^{131}I) or a placebo were given, other treatment was left to the physician in charge of the patients. Myxoedema appeared in 6 to 24 weeks. The usual symptoms appeared, and were easily treated by thyroid, but increase of dyspnoea often followed. The patients learned to regulate their own dose.

The clinical response was excellent in 7 (30%), good in 2 (9%), fair in 6 (26%) and poor or none in 8 (35%). 2 patients died during the study, one of pulmonary insufficiency and 1 of cerebral thrombosis following operation. 4 died subsequently, 3 from their cardio-pulmonary disease, and 1 of myocardial infarction.

The pulmonary function test results before and after treatment are given in a table, but the differences are not striking and the slight differences were not regularly in correlation with the clinical result. Interesting case reports are given. The reasons for success or failure in treatment in any particular patients are not clear, but if successful the results usually persisted. An allergic element was a favourable sign.

[This is a very interesting report of what appears to be a well carried out investigation and should be read in full. The treatment warrants further trial.]

F. H. Young

REEDER, L. G. **Occupation and Socioeconomic Status as Variables in Heart Disease Research: a Critique.** *Amer. J. Med. Sci.* 1959, Sept., v. 238, No. 3, 297–307. [27 refs.]

The author has reviewed 11 investigations, American and English, which are generally quoted on the relationship between heart disease and socio-economic status. The association was present in 9 of the enquiries and absent in 2. The overall picture drawn from these enquiries is rather confused. 2 definite explanations have been advanced for the relationship of the social class and coronary disease; one relates the disease with mental strain (in the professional classes) and the other to physical activity. Some studies have shown that the excess heart disease is due to specific occupations rather than to the social class as a whole. Within a social group it has been shown that the more sedentary occupations have the largest incidence, *i.e.* in one study bus drivers had more disease than bus conductors [this *Bulletin*, 1955, v. 30, 138] but in another investigation where this association was observed a further breakdown into town and country employees showed that the town conductors had a higher incidence of coronary disease than the country drivers. Most of the American studies were based on small selected populations and the author criticizes the method employed and the lack of appreciation of the concept of the socio-economic status and he suggests methods by which it should be possible to develop a sociological analysis to test the clinically observed associations.

W. J. Martin

ÖDEGAARD, A. Arbeidsdygtighet hos pasienter med angina pectoris. [**Fitness for Work of Angina Pectoris Patients.**] *Tidsskr. f. d. Norske Laegeforening.* 1959, Aug. 15, v. 79, No. 16, 950–51. English summary.

In all the 650 cases dealt with in this study, angina pectoris or infarct of the heart was diagnosed in Medical Department A of the Rikshospital in Oslo. All the patients were put on permanent anticoagulation treatment, and to each of them a questionary was addressed concerning their health and working capacity. The diagnoses dated from 1949 to the autumn of 1958, and the treatment given had lasted at least half a year. The men were classed in 3 groups according as their work was heavy, moderately heavy or sedentary, and the women in 2 groups according as their work was domestic or otherwise. Heavy work was manual, moderately heavy work was the work of shop assistants and salesmen, and sedentary work was office work and the sphere of higher education. Fitness for work was classified in 3 groups according as the patients were perfectly, imperfectly or not at all fit for work. 650 persons received the questionary and 627 answered it satisfactorily. From their answers, analysed in 5 different tables, it transpired that more than two-thirds of the patients had been able to carry on as before at work for many years, and that unfitness for work had been 4 times as common among heavy workers as among sedentary workers. Ödegaard wonders how or why one-quarter to one-third of his patients became unfit for work. The reason was plain enough when heart failure set in, but this was the case only in a minority. The big majority was composed of the patients who had noticed that work provoked angina pectoris pain or diffuse symptoms of a more vague character suggestive of a neurosis. Here the medical profession is apt to sin by coddling the patient. Ödegaard appeals to employers to do more than they have done in the past in adjusting the work of their employees to their limited capabilities.

Claud Lillingston

See also p. 17, FLETCHER, ELMES, FAIRBAIRN and WOOD, **The Significance of Respiratory Symptoms and the Diagnosis of Chronic Bronchitis in a Working Population.**

CANCER

GOODHART, C. B. **Cancer-Proneness and Lung Cancer.** *Practitioner.* 1959, May, v. 182, No. 1091, 578–84. [10 refs.]

There can be no reasonable doubt that cigarette smoking is a principal external cause of lung cancer, but it cannot be assumed that the loss of expectation of life due to this cause is necessarily equal to the normal expectation of life at the age at which lung cancer subjects die of the disease. If people are genetically different in their susceptibility to cancer, it would follow that those who die of lung cancer are "cancer-prone" and their expectation of life might be substantially less than normal.

Experimental studies have demonstrated that cancer has a genetic basis in many animal species and it is reasonable to assume that the same is true for man. This cannot be proved experimentally but there is some human evidence to support the assumption. For example, the mortality from cancer of one site varies greatly between different parts of Britain and between different London boroughs, but the range of mortality from all types of cancer is small. Similarly the incidences of breast and uterine cancer in different groups of women are inversely related and the great increase in lung cancer mortality over the last 25 years has been largely compensated for by a decrease in the mortality from other types.

If the hypothesis of cancer-proneness is correct, the mortality from all cancers, standardized for age, should be lower in non-smokers than in smokers and the observation that there is a difference in this respect does not invalidate the hypothesis. The hypothesis could, however, be tested by a more detailed analysis of the data obtained in the Medical Research Council's prospective study of smoking habits and mortality among doctors, by calculating the number of years by which the deaths of non-smokers who died of cancer could be regarded as being postponed so as to equate the total cancer death rates of smokers and non-smokers. A calculation of this type would give a truer measure of what is being risked by cigarette smokers. *Richard Doll*

DORN, H. F. **Tobacco Consumption and Mortality from Cancer and other Diseases.** *Pub. Health Rep.* Wash. 1959, July, v. 74, No. 7, 581–93, 7 figs.

A questionnaire about the use of tobacco, occupation and residence was sent to the holders of U.S. Government life insurance policies, who had served in the U.S. Armed Forces between 1917 and 1940. Usable replies were received from nearly 200,000 persons. The causes of death among this group in a period of 2½ years have been recorded and mortality rates calculated for the different groups of smokers and non-smokers. The causes of death were obtained initially from the death certificates, but more detailed information was also obtained by direct inquiry.

The death rate from all causes among men who had at any time regularly smoked tobacco was 32% greater than for men who had never smoked. Men who had smoked regularly only cigarettes had a higher death rate (58% above that among non-smokers) than other groups of smokers. For men who had smoked regularly only cigars or a pipe or both, the death rate was not appreciably greater than for non-smokers. Regular cigarette smokers who had stopped smoking before the study began had a death rate 39% higher than that for non-smokers, but this rate was substantially lower than that for men who had continued to smoke (65% greater than for non-smokers). The excess mortality among men who regularly smoked only cigarettes increased progressively with the amount smoked (29% for less than 10 cigarettes a day, 66% for 10 to 20 a day, 77% for 21 to 39 a day and 99% for 40 or more a day). Among pipe and cigar smokers an excess mortality was recorded only for men in the heaviest smoking category (20 or more pipefuls or 9 or more cigars a day).

The greatest increase in risk among smokers was recorded for cancer of the lung. Among regular cigarette smokers the risk was increased 10 times; among men who regularly smoked more than 20 cigarettes a day it was increased 16 times. For regular smokers of pipes and cigars the increase in risk was very much less. Regular cigarette smokers were also subject to an increased risk of dying from bronchitis, emphysema and certain other respiratory diseases (3·3 times), cirrhosis of the liver (3·0 times), gastric and duodenal ulcer (2·8 times), cancer of the buccal cavity and oesophagus (2·2 times) and cancer of the prostate (2·2 times). For other diseases the risk was either not increased or was increased less than twice. The leading cause of death among the policy holders was coronary heart disease; although the increase in risk for regular cigarette smokers was only 63%, coronary artery disease accounted for 45% of their excess deaths in comparison with non-smokers. *Richard Doll*

LINDSEY, A. J. **The Composition of Cigarette Smoke: Studies on Stubs and Tips.** *Brit. J. Cancer.* 1959, June, v. 13, No. 2, 195–9, 1 fig.

Studies have been made of the total amounts of condensable smoke produced at various stages in the mechanical smoking of cigarettes. It is found that the amount of condensable matter in mainstream smoke varies with the length of the stub and increases rapidly as the cigarette is smoked beyond the last 25 mm. Large amounts of condensable matter are also retained in the stub. These findings are in harmony with the idea of a repetitive process of distillation when suction is applied to the cigarette, followed by partial condensation in the remaining part of the cigarette.

Analysis of the smoke from cigarettes smoked to different lengths of stub showed that the amount of 3:4-benzpyrene was about 4 times as much when the cigarette was smoked to 15 mm. as when it was smoked to 35 mm. The difference in the amounts of some of the lower molecular weight hydrocarbons was very much less. Paper filter tips retained less polycyclic aromatic hydrocarbons than stubs of similar length.

Examination of the hydrocarbon content of stubs of cigarettes which had been smoked by a random sample

of the population gave somewhat different results, but many of them had been smoked to smaller stubs and there was a 6 months' delay between collection and analysis.

The results of these studies provide an explanation for the correlation between stub length and lung cancer mortality observed in some countries. [See also this *Bulletin*, 1959, v. 34, 540.] *Richard Doll*

Ahlmann, J. **Detection of Polycyclic Aromatic Hydrocarbons in Cigarette Tar.** *Acta Path. et Microb. Scandinavica.* 1958, v. 43, No. 4, 379–90, 9 figs. [32 refs.]

"1. A suitable combination of column chromatography and paper chromatography has resulted in an extensive fractionation of the neutral and acid fraction of cigarette tar—the fraction which contains the majority of the polycyclic aromatic hydrocarbons occurring in cigarette tar.

"2. The presence of 38 different compounds has been ascertained, 28 of these having been identified by means of absorption spectrophotometry.

"3. Among the compounds the following may be mentioned: 3.4-benzpyrene, 1.2 benzanthracene and 6.7-cyclopenteno-1.2-benzanthracene, which are all compounds with known carcinogenic action."

Borneff, J. & Knerr, R. Cancerogene Substanzen in Wasser und Boden. II. Das Verhalten von 3,4-Benzpyren unter Lichteinwirkung. [**Carcinogenic Substances in Water and Soil. II. Behaviour of 3,-4-Benzpyrene on Exposure to Light**] *Arch f. Hyg. u. Bakt.* 1959, Sept., v. 143, No. 6, 405–15, 4 figs. [25 refs.]

In this paper which follows a previous communication by the same authors [this *Bulletin*, 1959, v. 34, 1123] there is a description of experiments undertaken to study the decomposition by exposure to light of 3,4-benzpyrene which is known to be carcinogenic and to be present in the atmosphere under certain conditions.

A detailed account of the experiments is given here and of their results which are also discussed. It was found that 3,4-benzpyrene is sensitive to light, being destroyed particularly by short-wave ultraviolet light. This decomposition is greatest when the substance is exposed in a watery detergent solution but less in an oily solution and least of all when in crystalline form. It is estimated that daylight destroys between 20 and 50% of the benzpyrene which may be added daily to the atmosphere under certain conditions. *M. E. Delafield*

See also p. 26, Baetjer, Lowney, Steffee & Budacz, **Effect of Chromium on Incidence of Lung Tumors in Mice and Rats.**

See also p. 26, Hueper & Payne, **Experimental Cancers in Rats produced by Chromium Compounds and their Significance to Industry and Public Health.**

See also p. 16, Hendricks; Berry; Lione; Thorpe; Denholme, **Cancer of the Scrotum in Wax Pressmen. I. Epidemiology. II. Clinical Observations.**

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Atmospheric Pollution; Port, Ship and Aviation Hygiene; Infestation.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

Spaander, P. & Roest, A. C. F. **The Detection of Faecal Streptococci in Drinking-Water.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 2, 169–78. [11 refs.]

The difficulties in interpretation of differential tests for enterococci are outlined. Many of the difficulties associated with the Sherman tests are considered to arise because many of these are marginal tests. In the Netherlands the production of black colonies on sorbitol-tellurite-agar is recommended as a differential test but this again is sometimes doubtful in interpretation when colonies of all shades of grey are produced.

A citrate utilization test is recommended as an additional criterion in doubtful cases. A peptone water containing 1% sodium citrate at *p*H 7·4 is incubated at 37°C. for 48 hours. On adding 0·5 ml. of saturated lead acetate solution to 3 and 4 ml. of the culture a heavy precipitate occurs if the citrate has not been utilized and only a slight precipitate if the citrate has been utilized.

Tests with 55 known enterococcus strains gave positive results with all varieties of *Streptococcus faecalis*, negative results with *Str. bovis, Str. durans* and *Str. lactis* and variable results with *Str. faecium*. Of 8 strains of the latter examined, 7 grew with grey colonies on the tellurite agar, 5 of which were negative on citrate and 2 positive.

The examination of 200 strains of aquatic streptococci indicated that citrate utilization in conjunction with sorbitol-tellurite-agar enabled a reliable interpretation of faecal streptococci to be made. *E. Windle Taylor*

KATUGAMPOLA, D. C. & ASSIM, T. H. **Coliform Organisms in Domestic Water Supplies in Ceylon.** *Ceylon J. Med. Sci.* (Sect. D.) 1958, Feb., v. 9, Pt. 2, 95–103. [16 refs.]

The possibility of differentiating *Escherichia coli* from coliform organisms by using MacConkey broth or brilliant green bile broth at 44°C. in conjunction with indole tests at 44°C. was studied on 153 water samples in Ceylon. Of the samples giving positive results at 44°C. on MacConkey broth only 50% were *E. coli* I and similarly with BGB only 55·5% were *E. coli* I. *Klebsiella aerogenes* I accounted for 77% and 58% respectively of the remainder. Of other types all those which gave indole at 37°C. also produced it at 44°C., namely *K. aerogenes* II, *Citrobacter freundii* II and Irregular VII. These formed 8% of the total colonies fermenting lactose at 44°C. Under Ceylon conditions therefore a combined test using fermentation of lactose and indole production at 44°C. does not differentiate *E. coli* I absolutely from other coliforms.

The high proportion of *K. aerogenes* I strains positive at 44°C. may be due to their possible faecal origin in the tropics or to environmental and climatic adaptation of the organism outside the body. Standards for evaluation of tropical water supplies will not be satisfactory without further knowledge of the significance of these organisms. *E. Windle Taylor*

BRAZIS, A. R., BRYANT, A. R., LESLIE, J. E., WOODWARD, R. L. & KABLER, P. W. **Effectiveness of Halogens or Halogen Compounds in detoxifying** *Clostridium botulinum* **Toxins.** *J. Amer. Water Works Ass.* 1959, July, v. 51, No. 7, 902–12, 2 figs. [12 refs.]

Normally the toxins of *Clostridium botulinum* are not present in water and therefore are not considered as health hazards in public water supplies. The study reported by these workers was undertaken to find suitable methods of protection against possible contamination of water with these potent substances.

Partially purified and pure forms of *Cl. botulinum* Types A, B, C, D, and E, were used. It was found that the relationship between the survival time of mice injected with toxin and the toxin dose was sufficiently reproducible to serve as a method of assay.

The effect of the following halogen substances upon the rate of inactivation of Type A toxin was observed:— free available chlorine, mono-chloramine, mixed chloramines, iodine and chlorine dioxide. Types B, C, and D were studied only in relation to free chlorine and Type E was studied in relation to free chlorine and chlorine dioxide.

Inactivation of *Cl. botulinum* toxins by free available chlorine by the order of 1,000–10,000-fold is successful with concentrations of at least 0·5 mgm. per litre. The destruction was complete to the extent mentioned within one minute.

Chloramines are relatively ineffective in destroying *Cl. botulinum* toxins but iodine appeared to be effective in more alkaline solutions.

Chlorine dioxide however appeared to be superior to free chlorine, but difficulties with its estimation and uncertainty of its bactericidal effect make it unwise to recommend its use in place of free chlorine for inactivation of *Cl. botulinum* toxins.

Dosage of chlorine to maintain a residual of free available chlorine of 0·5 mgm./litre at the waterworks is well within the scope of the water industry but the maintenance of this concentration in the distribution system is a more difficult problem. *E. Windle Taylor*

FITZGERALD, G. P. **Bactericidal and Algicidal Properties of some Algicides for Swimming Pools.** *Applied Microbiol.* Baltimore. 1959, July, v. 7, No. 4, 205–11. [25 refs.]

This is a report on tests of the bactericidal and algicidal properties of some common chemicals and commercial chemical products used to control contamination in swimming pools.

Bactericidal tests were made at 23–26°C. with a reaction time of 1 hour to demonstrate the effect on an experimental source of infection, namely, settled sewage.

Algicidal tests extended over a period of 30 days with 3 types of algae, namely, a species of *Chlorella*, a blue-green species of *Oscillatoria* and a species of *Phormidium*. 6 commercial algicides were examined, all of American origin, but the exact composition of each was not divulged. The majority probably contained quaternary ammonium compounds, and they were named Algimycin, Algae-Nox, Exalgae, Algae-Kill, Hyamine-2389 and Berkite No. 4.

There is much advantage in employing an agent which is bactericidal as well as algicidal and so far as the bacteriological tests were concerned the experiments were carried out in conditions such as might prevail in a swimming pool with a maintained free residual chlorine figure of 0·5–1·0 mgm./litre. On the basis of the results obtained the chemicals could be ranked as to their bactericidal properties in the following order:—Algimycin, chlorine, Algae-Nox, Exalgae, copper, Algae-Kill, Hyamine-2389 and Berkite No. 4.

The algicidal properties of the compounds were examined with an initial killing dose and with a weekly dose to maintain control of the algae. The order of algicidal properties was almost the same as that for bactericidal properties. Copper, surprisingly enough, was required at a concentration of 6 mgm./litre, which corresponds to 24 mgm./litre of commercial copper sulphate ($CuSO_4 \cdot 5H_2O$). Such high concentrations would have other effects and are therefore not recommended for swimming pools.

The general conclusions of these tests and of others are that chemicals used in swimming pools for the control of algae display bactericidal as well as algicidal properties. Thus they would maintain bacterial control in circumstances where a free chlorine residual could not be kept on a 24-hour basis. The doses of these chemicals vary from 5 to 20 mgm./litre for an initial dose and 1 to 5 mgm./litre for subsequent weekly doses. *E. Windle Taylor*

CHOLAK, J. **Fluorides: A Critical Review. I. The Occurrence of Fluoride in Air, Food, and Water.** *J. Occupational Med.* Chicago. 1959, Sept., v. 1, No. 9, 501–11. [208 refs.]

ATMOSPHERIC POLLUTION

PATTLE, R. E., WEDD, G. D. & BURGESS, F. **The Acute Toxic Effects of Black Smoke.** *Brit. J. Indust. Med.* 1959, July, v. 16, No. 3, 216–20. [11 refs.]

In this interesting and valuable paper the authors describe experiments in which rats, mice and guineapigs were exposed to high concentrations of black smoke. The median dosages to death (Ct)D50 [see Pattle and Burgess, this *Bulletin*, 1957, v. 32, 977; *J. Path Bact.*, 1957, v. 73, 411] were measured, and the causes of death investigated.

Smoke was generated by burning tetralin in an open hurricane lamp, and was sampled on filter paper for estimation by weighing. The animals were kept in cages in a chamber containing the lamp. In most experiments they were kept separately, but in some a whole batch was kept in one cage. Sometimes they were exposed until all had died, and sometimes the survivors of initial exposure were withdrawn in order to find out whether delayed death occurred. Apart from those which died within 24 hours of ending exposure none died within the following month; for mice the risk seemed to end with the exposure, but 3 out of 10 guineapigs died in the following 22 hours. With guineapigs moreover the lungs contained numerous haemorrhagic, atelectatic patches which were larger in the animals which had survived longer, whereas with mice and rats there was neither oedema nor widespread atelectasis and death seemed due to blocking of air passages by carbon particles or by a secretion due to them. Animals caged together resisted smoke better than those caged alone; subsidiary experiments showed this to be due to their huddling together, the air breathed by one being filtered through its neighbour's fur.

Similar experiments with smoke from burning kerosene or coal distillates and from a diesel engine are mentioned. Despite the presence of up to 20 p.p.m. of sulphur dioxide in some instances the results were similar to those with pure smoke.

The results are discussed, in particular in relation to air pollution. The authors compare their data with those of WEEDON, HARTZELL and SETTERSTROM (*Contrib. Boyce Thompson Inst.*, 1939, v. 10, 281) and of Pattle and Burgess [see above] for sulphur dioxide, with which gas a third of the deaths took place after exposure had ended and late deaths were as common among mice as among guineapigs. Moreover judged by the 50% lethal dosage (L(Ct)50) tetralin is 10 times more toxic to mice and 25 times more toxic to guineapigs than SO_2. In the London fog of 1952 SCOTT [quoted in *Lancet*, 1953, v. 1, 288; see also this *Bulletin*, 1953, v. 28, 893] reported rather higher concentrations of smoke than of SO_2. The authors nevertheless warn the reader against drawing hasty conclusions about what was the main toxic agent in the 1952 smog since city smoke is different from tetralin smoke, the experimental concentrations were very much higher, and SO_2 sometimes has a bronchoconstrictive effect at concentrations at which there is no evidence that tetralin smoke is toxic.

J. McK. Ellison

GORHAM, E **Pneumonia and Atmospheric Sulphate Deposit.** *Lancet.* 1959, Sept. 5, 287–8, 1 fig.

Pneumonia mortality rates were calculated for the whole populations of 53 county and Metropolitan boroughs in England, Scotland and Wales for 1950–1954 and were plotted against the 1955 values of various constituents of deposited atmospheric pollution. Only sulphate deposit showed any obvious relation to pneumonia mortality, and the correlation coefficient between their logarithms was highly significant ($r = +0{\cdot}35$; $P = 0{\cdot}01$).

J. McK. Ellison

GOLDSMITH, J. R. & ROGERS, L. H. **Health Hazards of Automobile Exhaust.** *Pub. Health Rep.* Wash. 1959, June, v. 74, No. 6, 551–8. [32 refs.]

In most urban areas air pollution from spark-fired internal combustion engines is substantially greater than that from diesel engines (in Los Angeles about 20 tons of organic substances are emitted daily from the latter against 1,200 tons from the former). During normal running internal combustion engines do not completely burn petroleum and the exhaust gases contain oxides of nitrogen, carbon monoxide, hydrogen, aldehydes and unburned hydrocarbons in addition to carbon dioxide and water. Variable quantities of oxides of sulphur and of lead compounds are also usually present. The gases are rapidly diluted in the atmosphere and the concentrations present are determined by meteorological conditions as well as by the density of the traffic. For most of the pollutants there are agreed thresholds, below which no harmful effects are believed to occur under conditions of normal industrial employment. These limits are above the values observed at major road intersections, but that does not mean that automobile fumes are necessarily harmless. The various substances may act synergically and their combined effect on a respiratory invalid may be different from the sum of their individual effects on a healthy person.

For every part per million of CO which reaches the lung, it is calculated that 0·16% of the body's haemoglobin is inactivated. Maximum figures of 93 p.p.m. of CO have been recorded in the atmosphere, but more usual figures correspond to between 4 and 8 p.p.m. Cigarette smoking adds to this level and in urban smokers up to 8% of their haemoglobin may be inactivated.

Part of the nitric oxide emitted in the exhaust is oxidized to nitrogen dioxide and both compounds are present as pollutants. When the concentration of CO is 50 p.p.m. in the atmosphere, the concentration of nitrogen oxides may be about 1 p.p.m. Both nitrogen oxides interfere with oxygen transference (partly through the production of methaemoglobin) and will, therefore, exacerbate the effect of CO. In the U.S.A. lead tetraethyl is added to petrols in amounts of up to 3 ml. per gallon and average values of 7 μgm. of particulate lead per m^3 have been found in the air at Los Angeles. This small amount may be important to the individual when

added to the exposure met with in industry. The significance of the minute amounts of polycyclic hydrocarbons —including 3:4-benzpyrene—that are released into the atmosphere is difficult to assess; but they may play some part in the production of lung cancer. The quantity released by automobiles is very much less than that produced by the combustion of coal in towns where coal is a major fuel (*e.g.* London).

Where weather conditions lead to poor dispersal and there is much solar radiation, an interaction of nitrogen oxides and hydrocarbons produces "photochemical smog", containing ozone and organic intermediates. Eye irritation is common, but although the concentration of ozone may exceed the standard set for industrial exposure (0·1 p.p.m.), it is not clear whether the recorded amounts can irritate the respiratory tract in man.

Richard Doll

GOETZ, A. & TSUNEISHI, N. **A Bacteriological Irritation Analogue for Aerosols.** *Arch. Indust. Health. Chicago.* 1959, Aug., v. 20, No. 2, 167–80, 12 figs.

The aim of the experiment described was to find out whether the irritant properties of an aerosol could be measured by the extent to which it inhibited the growth of a bacterial culture. In the method used a uniform or a logarithmically graded deposit of bacteria (*Escherischia coli*) is filtered on to a membrane and the aerosol deposited on it by means of a rotary impactor. The membrane is then "developed" by placing on a nutrient pad, incubating, and staining with methylene blue. Both rotary impactor and the preparation of the deposits of bacteria are described, and some results are given.

The rotary impactor consists essentially of a drum round which the membrane is stretched taut. The drum rotates slowly about its axis, and the aerosol is directed on to the membrance through a slit. The velocity of impaction is normally 56 m./sec.; the distance between slit and membrane is not stated. The authors claim that with this method of impaction the halo-like secondary pattern given by plane surface impingers is absent, but this claim is not borne out by the figure shown (figure 4b). The "concentrometer" used for preparing the graded deposit of bacteria and the method of generating test aerosols are also described.

The apparatus was used to carry out bacteriological irritation analogue (BIA) tests on irradiated automobile exhaust, tobacco smoke and synthetic aerosols. The results show that irritant vapours cause little or no inhibition of bacterial growth unless aerosols are present, but that relatively non-irritant aerosols such as tobacco smoke are also highly inhibitory. The preliminary results are discussed.

[This interesting paper is marred by lack of care in preparation and correction.] *J. McK. Ellison*

PORT, SHIP AND AVIATION HYGIENE

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. No. 174. **Expert Committee on Hygiene and Sanitation in Aviation. First Report.** Geneva, 10–15 March, 1958. 62 pp. [28 refs.] 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

In 1950 the International Air Transport Association brought to the notice of the World Health Organization the need for improved airport sanitation for the protection of aircrews and passengers against diseases other than those of the quarantine group, in particular those of sudden onset, such as acute gastro-enteritis and food poisoning, which might seriously endanger the efficiency of the crew and the safety of the aircraft.

The existing International Sanitary Regulations are directed specifically to control or limit the spread of the 6 quarantinable diseases—cholera, plague, smallpox, yellow fever and louse-borne typhus and relapsing fever. Though these regulations have been accepted internationally, the World Health Organization has no responsibility for enforcing the necessary health regulations. The International Sanitary Regulations are presented in broad terms, and there are no standards nor methods laid down to assist those who have to administer them. For instance, sanitary airports are required to have a "pure" water supply, but it is left to each country to decide what is the standard of purity and this varies greatly from one country to another.

The Fourth World Health Assembly, in 1951, recognized this need for improved environmental sanitary control in and around airports not only to facilitate the speedy transit of air traffic in the interest of world economic and social progress, but also in the interest of the health of the local populations. This Assembly also stressed the need for a manual which would set out the general sanitary safeguards that are reasonable to apply at airports as a guide to health agencies and operators responsible for the hygiene and sanitation of airports.

The World Health Organization Expert Committee on Hygiene and Sanitation in Aviation met in 1958 and considered the problems raised by the Assembly's resolutions, and reviewed the text of the *Guide to Hygiene* and *Sanitation in Aviation*, which is appended to their Report. This Report embodies the collective views of an international group of experts having special knowledge of airport administration, ground operations, facilitation, sanitary engineering, hygiene and aviation medicine. It does not, however, necessarily represent the decisions or the stated policy of the World Health Organization.

Among the many suggestions and recommendations made in this report are the following:

That all drinking-water supplies at airports should conform to the standard laid down in the WHO International Standards for Drinking-water (1958), and that their purity be checked bacteriologically at least once a week.

That all food-handling establishments at airports should be under proper public health supervision so as to provide safe food.

That insect breeding places, particularly those of mosquitoes and flies, in and adjacent to airports should

be eliminated, rather than that larviciding should be used, and that aircraft disinfection procedures should be of such a nature as not to delay scheduled operations. In addition, that research be encouraged to provide means of impregnating the fabrics of aircraft interiors with long lasting and effective residual insecticides and so do away with the need for aerosol spraying.

That consideration should be given to the establishment of a single organization at each airport to perform such sanitary services as the loading of potable water, removal of sewage and waste from aircraft, and general cleaning of the cabins, instead of each airline doing its own: this would standardize procedure, be an economy of manpower and reduce expenses.

That health authorities should pay particular attention to the need for the rapid and efficient performance of their various duties in connexion with the clearance of aircraft in order to curtail transit time to the minimum.

That the Facilitation Committee or similar panel at airports should devote more attention to health problems and, for this purpose, should have a representative of the health administration on their Committee.

That where a local health department is available to an airport, the responsibility for public health control within the airport and the contiguous area should come under the supervision of that authority, rather than burdening the airport authority with such duties. Similarly, the appropriate health authority should exercise sanitary supervision of transit areas, direct or indirect, including hotels where aircrew and passengers are accommodated, particularly as regards food-handling activities.

That consideration should be given to the utilization of airport quarantine officers by giving them certain responsibilities in connexion with the supervision of sanitation and hygiene at international airports.

That the WHO *Guide to Hygiene and Sanitation in Aviation* should be published in as many languages as possible and so illustrated as to convey essential practical points even to illiterate persons who may be engaged in important menial sanitary duties. Moreover, that it should have the widest possible circulation for the information and guidance of all concerned with airport hygiene and sanitation, and that it should form the basis of training of personnel in such matters.

That WHO should encourage regional and inter-regional seminars for representatives from national health administrations, airport operators, airlines, the International Civil Aviation Organization and the International Air Transport Association to disseminate the basic concepts contained in the *Guide to Hygiene and Sanitation in Aviation*, which should give flesh, blood and vitality to the bare bones of the International Sanitary Regulations of the World Health Organization.

H. E. Whittingham

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

MINISTRY OF LABOUR AND NATIONAL SERVICE. **Annual Report of the Chief Inspector of Factories for the Year 1958** [McCULLOUGH, T. W.]. Cmnd. 810. 95 pp. 1959. London: H.M. Stationery Office. [5s. 6d.]

One of the merits of the Annual Reports in their new form, started 2 years ago, is no doubt what the Chief Inspector, in presenting the 1958 Report, says of the reception given to the 1957 Report [this *Bulletin*, 1959, v. 34, 132]: he has been told by many directors and others that for the first time they were able to read the report in full, instead of reading selected passages. The Annual Report on the work of the Factory Inspectorate for the year 1958 has been prepared on the same lines but a change in accident classification is announced for the 1959 report. The Standard Industrial Classification (1958 revised edition) will also be used and some of the tables will be presented in new form. This method will provide a more up-to-date picture for accident prevention purposes, but will necessarily mean discontinuity. A list of publications on safety, health and welfare puts to good use the cover of the 1958 Report and 2 special subjects included in the Report are nuclear energy and ionizing radiations problems and fire prevention.

The Atomic Energy Research Establishment's full training course on reactors and isotopes has been taken by some Headquarters inspectors and a shorter course on ionizing radiations by other inspectors. Old problems are still met in the erection and operation of nuclear reactors: the new ways of meeting new hazards are described, *e.g.* electrical instrumentation and control, with a diversity and duplication of safeguards. The Atomic Energy Authority's organization for safety and health is made clear and also the Factory Inspectorate's active part in investigations. A section on sealed and open sources of radiation deals with processes, apparatus and isotopes and with difficulties and mishaps in the use of plant producing ionizing radiations. The Factories (Ionising Radiations) Special Regulations are being redrafted as a result of a number of comments.

One of the main objects of a Bill to amend the Factories Acts, 1937 and 1948, now referred to a Standing Committee, was to extend the fire safety provisions to

include fire prevention and fire fighting. These subjects are discussed from many angles: how fires start in factories; sources of ignition; how fires spread and how they could be limited. Obstructions to fire fighting are caused as much by failure to inform fire brigades beforehand of potentially dangerous materials as by the material itself or its location.

The number of factories decreased by 2,852 to 223,085 since 1957 even though the Slaughterhouses Act, 1958, brought additional places within the scope of the Factories Acts. Reported accidents decreased except in building operations and works of engineering construction. Reference is made to an increase in works transport accidents (except on works railways). Portable electric apparatus caused the greatest proportion of electrical accidents. Old established methods for guarding against accidents with overhead lines are described and advised even when new electrical warning devices are used.

Communication by radio, signalling systems for crane operations, tower cranes, fibre glass for painters' cradles and boatswains' chairs and the use of synthetic fibres for ropes, lifelines and safety-belts are among the developments discussed which solve or sometimes may add to safety problems. Precautions are listed for handling organic peroxides and mercury.

Throughout the report developments in the work of safety and health organizations, both in industry and outside it, and the Inspectorate's collaboration with research associations and committees in Britain and abroad, and, not least, safety training in technical colleges and schools are given the prominence they deserve.

M. Patricia Fitzsimons

MINISTRY OF LABOUR AND NATIONAL SERVICE. **Annual Report of the Chief Inspector of Factories on Industrial Health for the Year 1958** [MCCULLOUGH, T. W.]. Cmnd. 811. 61 pp. 1959. London: H.M. Stationery Office. [3s. 6d.]

Like its companion volume [the main Report, see above], the Annual Report on Industrial Health reviews events of the year 1958 and also 2 special subjects, occupational cancer and medical supervision in factories. Health problems, largely the province of the medical inspectors working in conjunction with other branches of the Inspectorate, are investigated with the help of Appointed Factory Doctors, industrial medical officers and nurses and other doctors concerned with occupational hygiene and research. It is pointed out, however, that doctors outside this specialized field could add much to the knowledge of health hazards by reporting to the medical inspectors cases in which occupational factors may be involved. The Inspectorate depends on notification, whether statutory or voluntary, of industrial diseases and gassing accidents as a means towards prevention, and every notified case is the subject of special investigation at the factory where the case occurred and possibly elsewhere. A new departure in factories legislation highlights such past work, limited as it necessarily was: a clause in the 1958 Factories Bill seeks to impose on the Minister a duty to promote health, safety and welfare by collecting and disseminating information and investigating such problems.

Compressed air illness is given some prominence as well as the Special Regulations which came into force during the year. A 1958 departmental memorandum on the medical aspects of work in compressed air excludes treatment which was to be the subject of a Medical Research Council statement. The Council's re-assessment of its 1952 recommendation that oxygen should be used by first-aiders in resuscitation of asphyxia is quoted: the use of 5% carbon dioxide in oxygen is now recommended for carbon monoxide poisoning, and for all other cases of asphyxia oxygen alone. A process recently introduced, "chromising", and an increasing use of beryllium in copper alloys are the subject of warning against dust or fume. The familiar statistical tables appear. Case histories of particular significance are described, among them poisoning by creosote, tetraethyl lead and phosdrin (2-methoxycarbonyl-1-methylvinyl dimethyl phosphate), the last capable of slow penetration of ordinary rubber gloves—polyvinyl chloride gloves appear to be more resistant. Tetrachloroethane caused a death from toxic jaundice, even though precautions were stringent and a man doing similar work remained healthy.

Much detail is compressed into a useful chapter on occupational cancer which deals with carcinogens, processes, industries, surveys, research, legislation, latent periods and methods of prevention.

A survey of arrangements for medical supervision was made in 210 factories, large, medium and small, in all parts of the country, excluding nationalized industries and government departments. The data and analyses accord well with ideals of industrial medicine. In estimating the relative value of various services, the medical inspectors found that medical examinations in one form or another ranked first in importance; advice about factory conditions second; and treatment of emergencies and minor illness third. The opinions of management on the advantages of medical supervision ranged remarkably, with 5 points predominating: saving of workers' and production time; beneficial effect on workers' morale; emergency treatment; advice about working conditions; and the value of medical examinations particularly with reference to selection. In 153 factories there was said to be some overlap with the National Health Service, mainly limited to minor treatment.

This report, with its references to publications, committees, people and case histories, is once more a mine of information for industrial medical officers and candidates for the Diploma in Industrial Health.

M. Patricia Fitzsimons

MATHIEU, C. & TRONCHE, R. Le problème du bruit en Médecine du Travail. [**The Problem of Noise in Industrial Medicine**] *Arch. Malad. Professionelles.* Paris. 1959, July–Aug., v. 20, No. 4, 374–95, 10 figs.

This paper goes into much detail about this scourge of modern life and into measures to control the incidence and degree of occupational deafness. The difficulties are recognized and overmuch discussion may have delayed action.

Definitions of noise and units of measurement are followed by a description of means of measurement and a table in which the noise levels in various occupations

are related to the possibility of conversation or communication or of ear damage. Sections on hearing and the action on it of noise, with a discussion on pure tone and vocal audiometry, lead on to an account of occupational deafness and of physiological, psychic, physical and psychosomatic effects. Details of noise suppressive measures and of individual protective appliances show that much is possible and that, faced with the infirmity of deafness, the inconveniences of protection must be accepted.

Difficulties raised when attempts are made to legislate for compensation to the civilian deafened by his work are shown to be magnified. For example, a diagnosis of occupational deafness can be made, particularly if an audiogram had been made on recruitment. Sound surveys would show which occupations or jobs carry the risk, *e.g.* where an individual is constantly exposed to 90 decibels or more. Without the necessity for sound meters and audiometers throughout industry, screening by the industrial medical officer, using a tuning fork [4,096 cycles] and his voice, would indicate whether audiometric examination was desirable. In 3 months, a reasonable qualifying period, it is possible to distinguish progressive impairment of hearing acuity. Other symptoms are uncommon enough or sufficiently reversible to be ignored in this context. For the calculation of disability rates the authors propose Mayer and Rey's table which is reproduced; this sets forth several hearing loss percentages based on the distance at which the voice is heard. *M. Patricia Fitzsimons*

AMERICAN INDUST. HYG. ASS. J. 1959, June, v. 20, No. 3, 249–57, **Hygienic Guide Series.**

The Hygienic Guide Series concerns chemical substances in industry and now consists of 78 guides the titles of which are stated. The individual guides are obtainable from the American Industrial Hygiene Association. In the present issue of the Journal of this Association there are set out detailed particulars contained in the Guides on (1) propylene oxide, (2) tetrahydrofuran (tetramethylene oxide), (3) polonium-210, (4) radon and its daughters, (5) selenium and compounds (excluding hydrogen selenide) and (6) titanium. Each substance is dealt with under the headings of:—I. *Hygienic Standards*—(a) recommended maximum atmospheric concentration, (b) severity of hazards to health or by fire, (c) short exposure tolerance and atmospheric concentration immediately hazardous to life; II. *Significant Properties*—chemical and physical data; III. *Industrial Hygiene Practice*—(a) recognition, (b) evaluation of exposures by direct instrumental methods and chemical analysis and (c) recommended control procedures; and IV. *Specific procedures* of control and of treatment of toxic effects by first aid and medical methods. To each guide an appendix of references is given.

M. E. Delafield

HARRIS, D. K. **Some Hazards in the Manufacture and Use of Plastics.** *Brit. J. Indust. Med.* 1959, July, v. 16, No. 3, 221–9, 2 figs. [72 refs.]

Bringing his 1953 review up to date [this *Bulletin*, 1954, v. 29, 177] the author gives much evidence of his wide experience, the organization in which he works being the largest single manufacturer of plastics raw materials in the Commonwealth. Plastics, whether raw material or finished products, designed to be food containers, should be free of constituents which could be extracted by their contents. Preliminary testing with solvents suggested by The British Plastics Federation is advised but results may indicate that prolonged pharmacological tests are necessary. Toxic properties of some stabilizers and chemicals used in manufacturing polyvinyl chloride compositions show why some should be excluded from contact with workpeople and food; alkyl tin compounds are examples, though the dioctyl and dinonyl derivatives are relatively harmless. New polyolefines are being produced: the catalysts, among them aluminium alkyl compounds, may be dangerous.

Polytetrafluoroethylene (Fluon) at high temperatures gives rise to decomposition products which may be harmful if inhaled. Rats exposed for 6 hours to fumes of Fluon heated to 250°C. showed no ill effects; at 275°C. they showed irritation but recovered and post-mortem examinations showed no abnormality; at 300°C. they died from pulmonary congestion and oedema.

Butadiene is combined in varying proportions with styrene, acrylonitrile or methyl methacrylate to produce many products. The toxic properties of these monomers is described. Butadiene copolymers are inert.

The successful use of certain plastics in orthopaedic, vascular and ophthalmic surgery is discussed. Tissue reactions have sometimes been due to misuse, *e.g.* weight-bearing, but though the effects of a few selected plastics have been investigated, the response of living tissues to implants will not be known for many years.

Though the investigations to ensure freedom from harm to those who make and use plastics have been thorough, they continue to be essential and manufacturers should have laboratory facilities and a technical service to deal with new problems. *M. Patricia Fitzsimons*

QUOOSS, H. Gesundheitsgefahren in der Kunststoffindustrie. [**Health Hazards in the Plastics Industry**] *Arbeitsmed.* 1959, No. 32, pp. v+82. [Numerous refs.]

This article is an exhaustive survey of the materials and processes involved in the manufacture of plastics, synthetic fabrics, adhesives, rubber and other synthetic articles, and of their hazards, actual and potential.

Among the *plasticizers*, tricresyl phosphate, and to a lesser degree, tributyl phosphate and 2-ethylhexyldiphenyl phosphate (Santiciser 141), carry the hazard of spastic paralysis, an action attributed to their inhibition of cholesterinase.

Phthalates and phthalic acid esters (Palatinols) are generally considered harmless in industrial use, but some have been found toxic to animals in high dosage. Butyl stearate and methoxyethyl stearate have an animal toxicity (keratitis and nephritis) similar to that of dibutyl phthalate; the chlorinated diphenyls, rarely recorded as industrial toxins, have a potential toxicity similar to that of the chlorinated naphthalenes (acne and liver injury). Citrates, dibutyl sebacate, ethyl hexyl adipate and the benzoic acid esters are practically non-toxic.

Of the glycol compounds, polypropylene glycol, methyl glycol, ethylene glycol monoethyl ether (cellosolve) and thioglycollic acid (also used as a "cold

wave" agent) are potentially toxic to eyes, kidneys and liver. Pigments and dyes are hazardous when inhaled as dust, from the point of view of their content of arsenic, copper, lead and antimony.

Fillers include some substances such as asbestos and quartz with a silicotic hazard; glass fibre causes skin irritation and "glass wool lung", with non-progressive X-ray striation.

Among the *solvents* used, those to be avoided whenever possible are benzene, carbon disulphide and carbon tetrachloride.

Foam materials may be produced by physical or chemical reactions. Poroflor-N(azoisobutyronitrile) the basic materials for which are sodium cyanide, hydrazine sulphate and acetone, forms a decomposition product, tetramethyl dinitrile succinic acid, which is lethal to animals in a concentration of 6 p.p.m. A syndrome of nervous and digestive disorder in industrial workers who cut the finished material into strips and sew these into linings for waterproof garments is described in detail in 13 cases and is attributed to the evolution of this compound when the foam material becomes overheated during manipulation with blunt tools.

Diazoaminobenzol is said to have caused skin lesions, and aniline is one of its decomposition products. Benzolsulphohydrazide, dinitroso-pentamethylene-tetramine and azo-dicarbonic derivatives are harmless.

Resins carry as their main hazard skin irritation and sensitization, the latter especially with formalin resins. "Bakelite itch" is attributed chiefly to formaldehyde, but phenol may be partly responsible. Workers employed on pressing machines complain also of headache, irritability, weakness, poor appetite and dry cough.

Formaldehyde resins are used in lamination processes and are contained in many adhesives, which may provoke the same reactions.

Urea formaldehyde resins are used in textile finishing, sometimes combined with pyridine, to which digestive disturbances and changes in the differential blood count are attributed.

The outstanding risk of the epoxy resins, produced by the condensation of epichlorhydrine and phenol derivatives, is dermatitis; it is lessened by keeping the temperature low during manufacture. Allyl alcohol, a basic material for polyester resins, is a strong corrosive to skin and a severe eye irritant; benzoyl peroxide, used as a hardener, also causes dermatitis and eye injury.

In the manufacture of *polyethylenes*, the chief basic material for polymerization is ethylene, and catalysts are mainly alkyl aluminium compounds; these have a corrosive action on the skin, and aluminium chloride, used also in the production of lubricating oils, may cause spasmodic bronchitis. In the production of polyvinyl chloride from vinyl chloride, dichloroethane, with a toxic hazard similar to that of carbon tetrachloride, is an intermediate product.

Stabilizers include compounds of lead, tin, barium and cadmium, alphanaphthylamine, paraphenylenediamine, dimethyl aniline, ethylene oxide and trimethylamine, the last may cause skin injury.

Polymerized synthetic materials are devoid of toxicity in their finished state, but symptoms of upper respiratory irritation, chronic gastritis, hepatitis and low haemoglobin values have been reported from exposure to polyvinyl chloride dust; these are attributed to the chlorinated plasticizers.

Styrene (vinyl benzol), liberated when polystyrene mixtures are overheated, has proved toxic to animals, and has caused respiratory and nervous symptoms in human beings. The evidence for 1 fatal case of lymphoblastic sarcoma of the intestine is not conclusive.

Fluorinated compounds (Teflon, Fluon, Hostaflon), if decomposed by heat, give off gases causing symptoms similar to metal fume fever; continued exposure may result in oedema of the lungs.

Polymetacrylic esters, the basis of Plexiglas, are irritant to skin and mucous membranes; an intermediate product, acetonecyanhydrin, is a highly toxic agent with a cyanide-like effect, and acryl nitrile (vinyl cyanide) used especially in the manufacture of synthetic fibres, may be metabolized with formation of cyanic acid. The chief solvents associated with the acryl nitriles are dimethyl formamide, with toxic properties similar to those of carbon tetrachloride, and dimethyl sulphoxide, so far not reported as toxic. Chloracrylates and α-β dichloropropionic esters cause blistering of the skin and possibly lung oedema.

Polyamides, with a basic material hexamethylenediamine, are used in the manufacture of nylon and Perlon. Caprolactam is relatively non-toxic but has caused some cases of respiratory catarrh, digestive disturbance and eczema of the hands.

Isocyanates, used chiefly in lacquers and adhesives, are irritant to the skin and respiratory system, causing asthmatic attacks. The most toxic in present use is toluylene diisocyanate (Desmodur T).

Silicones are generally only slightly toxic, but when burnt decompose into silicium dioxide; when used as fillers they carry a risk of silicosis, and as sprays in impregnation materials can cause pneumothorax and emphysema. Chlorosilanes are highly corrosive to skin and eyes; oxysilane, though less toxic in this respect, is synthesized from benzol and bromine and thus carries a benzol hazard.

In the manufacture of *synthetic rubber* butadiene is of low toxicity; chloroprene has caused lassitude, chest symptoms and loss of hair.

Special risks are those associated with the use of radioactive catalysts and of potential carcinogenesis from inhalation of the dust of certain synthetic materials with a high chlorine content, though no specific component has been identified as responsible. Recently 2 epoxy compounds—vinyl cyclohexene dioxide and butadiene dioxide—have been incriminated.

For full details of all the compounds and processes described the original article should be consulted; it is too long to be abstracted completely satisfactorily.

Ethel Browning

HENDRICKS, N. V.; BERRY, C. M.; LIONE, J. G.; THORPE, J. J.; DENHOLM, J. S. **Cancer of the Scrotum in Wax Pressmen. I. Epidemiology** [HENDRICKS, BERRY, LIONE & THORPE]. *Arch. Indust. Health.* Chicago. 1959, May, v. 19, No. 5, 524–9, 5 figs. [11 refs.] **II. Clinical Observations** [LIONE & DENHOLM]. *Ibid.*, 530–39, 7 figs. (5 coloured on pl.).

I. The study was begun because a review of all the cancer cases from an oil refinery where wax was

manufactured revealed 2 cases of scrotal cancer. To obtain sufficient data the industrial records for the previous 10 years were reviewed and the refinery workers were observed for a further 10 years. Over the whole period the average annual cancer incidence among an average of 2,630 refinery workers was 339 per 100,000, which was very close to the age-adjusted incidence reported for the general white population at the mid point of the study (*i.e.* 336 per 100,000). The incidence was higher among the group of men who had worked for 10 years or more in wax manufacturing (563 per 100,000) and much higher among the subgroup of 82 men who had worked for 10 years or more as wax pressmen (1,393 per 100,000). 18 cancers in all were reported among this last group and 11 of them were scrotal in origin. It is estimated that the incidence of scrotal cancer was some 5,000 times normal, whereas the incidence of all other cancers was close to normal. No scrotal cancers were reported among men with less than 10 years' employment as wax pressmen.

In the process of preparation a distillate containing about 8% wax was first obtained from the crude oil by fractional distillation. The wax was removed from solution by chilling and was then separated from the oil by pressure. The crude or "slack" wax so obtained contained 20–40% of oil distillate and this portion contained 7–25% of aromatic-type compounds and has been shown to be carcinogenic to animals [this *Bulletin*, 1952, v. 27, 265]. The pressmen separated the wax from the plates by means of iron bars and in so doing their clothing became saturated with oil distillate. Since 1950 a new process has been instituted which eliminates routine contact with the crude wax.

II. Clinical case histories are given for 10 of the 11 cases of scrotal cancer that occurred among the group of 82 wax pressmen. The age at diagnosis ranged from 47 to 62 years and the duration of possible exposure to the wax ranged from 14 to 37 years. A primary lesion was observed 2 years after cessation of contact with the wax and a recurrent lesion was noted after 10 years; it is recommended that workers with a history of exposure should be examined at 3-month intervals for the rest of their lives. 2 subjects died of the disease; 2 died of other causes 2 years and 6 years after diagnosis respectively and six were living 3 to 14 years after the diagnosis was first made. *Richard Doll*

FLETCHER, C. M., ELMES, P. C., FAIRBAIRN, A. S. & WOOD, C. H. **The Significance of Respiratory Symptoms and the Diagnosis of Chronic Bronchitis in a Working Population.** *Brit. Med. J.* 1959, Aug. 29, 257–66, 2 figs. [23 refs.]

The term bronchitis indicates an inflammation of the mucous membrane of the bronchi, of non-specific aetiology. As the presence of this inflammation cannot readily be established in life, the disease must in practice be defined and diagnosed upon the symptomatic consequences of the inflammation—namely chronic cough and expectoration (when other causes of these symptoms have been excluded). Some clinicians submit that chronic cough and expectoration do not by themselves justify a diagnosis of chronic bronchitis but that in addition there should be evidence of discomfort, if not disability, due to breathlessness. Others seeking to identify the "earliest phase" so as to prevent progression emphasize the need to regard cough and sputum as adequate evidence of bronchitis [this *Bulletin*, 1956, v. 31, 1234].

Fletcher and his colleagues examined this diagnostic dilemma in a carefully planned study among 2 groups of post-office workers in London. 192 postmen, aged 40–59, and 192 women in the same age-group employed indoors in the Post Office Savings Branch were the subjects of comparison.

Each person was asked to complete a questionary (this is reproduced in the appendix to the paper) on cough, phlegm, breathlessness, influence of weather on chest, history of chest illness and smoking habits. Specimens of sputum were collected for inspection and examination on separate occasions in winter and summer months.

Measurements of the one-second forced expiratory volume ($FEV_{1\cdot0}$) were derived from tracings of expiration made on a light spirometer with a paper speed of 2 cm./sec. In the women additional measurements were made of peak expiratory flow with Wright's expiratory flowmeter. After standardization of $FEV_{1\cdot0}$ for various factors the indirect maximum breathing capacity (MBC) was calculated by multiplying by 35.

Analyses of the results, which are tabulated, showed that men had more cough and sputum than women, but the prevalence of other symptoms and of chest illnesses was similar in the two sexes. Symptoms increased with age in the men but not in the women. These differences were only partially attributable to differences in smoking habits. The following excerpt from the authors' summary merits quotation in full.

> "The severity of phlegm production was graded according to whether or not it occurred throughout the day, and this grading correlated well with the volume of sputum produced in the first hour after waking. Whether or not the phlegm was said to be perennial appeared not to matter. Ventilatory capacity was significantly impaired in the men, but not in the women, who had the higher grade of phlegm production, frequent wheezing, susceptibility to adverse weather, and a history of chest illnesses with an increase of phlegm production.
>
> "It is suggested that chronic bronchitis should be diagnosed in subjects with a productive cough not due to other causes, and that it should be graded in severity either according to the persistence of the symptom throughout the day or according to the volume of sputum expectorated. Disability from impairment of ventilatory capacity or recurrent chest illnesses should be regarded as complications, and not as essential features of chronic bronchitis, since it is important to recognize the disease before it has resulted in disability. Only prospective studies can determine the prognosis of the suggested grades of bronchitis in respect of the development of disability.
>
> "The disabling form of the disease can be referred to as 'chronic bronchitis with ventilatory impairment' and 'chronic bronchitis with recurrent exacerbations", and may be graded according to

the severity of the impairment and the frequency of exacerbations. Disability appears to be a less frequent consequence of chronic bronchitis in men than in women."

Comparison of the results with other surveys [*ibid.*, 1956, v. 31, 1234; 1958, v. 33, 238] was attempted but this proved difficult owing to different criteria used for diagnosis and the introduction of other considerations.

The authors conclude:

"*Chronic bronchitis may be defined as 'the production of phlegm on most days for at least three months in each year'.*"

[Since 1948 the Pneumoconiosis Research Unit at Cardiff have advocated with substantial success the use of an International Classification of Radiographs of the Pneumoconioses [see below p. 21] and the Thoracic Society [GANDEVIA and HUGH-JONES, *ibid.*, 1958, v. 33, 355] have recommended the need for a uniform terminology for measurements of ventilatory capacity. Chronic bronchitis among coal miners and iron and steel foundry workers is currently a highly controversial subject, which is likely to attract increasing research in the near future. If this should prove true is there not a like need to assure that at least all investigations should include an agreed standard questionary and programme of investigation to facilitate valid basic comparisons?] *A. Meiklejohn*

GUYTON, H. G., DECKER, H. M. & ANTON, G. T. **Emergency Respiratory Protection against Radiological and Biological Aerosols.** *Arch. Indust. Health.* Chicago. 1959, Aug., v. 20, No. 2, 91–5, 4 figs.

The object of this work was to test various articles which might be used as respiratory filters in emergency.

Cotton, paper and rayon clothing or household articles were tested for filtration efficiency and resistance to breathing. A suspension of the non-pathogenic spore-forming *Bacillus subtilis* var. *niger* was atomized under conditions which would simulate inhalation of dust, particulates being between 1 and 5μ in diameter. A mask evaluation mouth collector was fitted to each of 5 volunteers in one of the air locks. He applied a test article over the mouth sampler and entered the exposure chamber for 5 minutes' exposure to the spore aerosol. In the exit air locks the test articles were released and the absorbent packing was removed with aseptic precautions from the sampler cartridge.

High resistance to breathing limited the use of some of the 18 items, particularly when wet, the specifications of which appear in a table. A resistance of 36 mm.H_2O was the greatest that could be borne except for short periods, and it was considered doubtful whether women or children could tolerate for an indefinite period a resistance greater than 20 mm.

When wet, the only useful item was a bath towel, with resistance 3 mm. but filtration efficiency only 70·2%, the latter being less than with 7 dry articles though some of these had a high resistance, *e.g.* a fine muslin bed sheet, 131 threads per sq. inch, and a man's cotton handkerchief when crumpled or folded into 16 layers, 80 × 10 threads per sq. inch.

When dry, a filtration efficiency greater than 85% and a resistance less than 20 mm.H_2O were given by: the handkerchief folded in 8 layers; toilet tissue, 3 layers; and the bath towel in 2 layers.

M. Patricia Fitzsimons

BRINGHURST, L. S., BYRNE, R. N. & GERSHON-COHEN. **Respiratory Disease of Mushroom Workers. Farmer's Lung.** *J. Amer. Med. Ass.* 1959, Sept. 5, v. 171, No. 1, 15–18, 2 figs. [11 refs.]

A description is given of the clinical and radiological features of a respiratory disease which occurs amongst Puerto Rican migrants in Chester County, Pennsylvania, U.S.A., engaged in the making of composts for the purpose of mushroom growing. The symptoms of this disease developed promptly in these workers when they were exposed to materials undergoing composting during spring and autumn. They may include, during the acute phase: dyspnoea, nausea, vomiting, pain, cough, sputum, pyrexia, tachycardia and prostration. On the patient being removed from contact with the composting materials symptoms gradually subside but may recur on re-exposure. In some patients recurrent attacks are mild in comparison with the initial attacks. X-rays taken during the acute phase generally show diffuse infiltration of the lungs but occasionally scattered minute seedings or segmental infiltration. During the chronic phase X-ray findings usually suggest increased fibrosis. Resolution of these features is at first rapid and then lags after the clinical symptoms have subsided. Examination of the sputum from such patients does not reveal any aetiological agent.

It seems from this account that the disease from which these workers suffer is a form of farmer's lung although it is curious that it appears to be confined to Puerto Rican migrants. *C. J. La Touche*

OCCUPATIONAL DISEASES

WINKEL, A. Über eine neue Methode zur Staubmessung. [**A New Method of Measuring Dust**] *Staub.* Düsseldorf. 1959, July 1, v. 19, No. 7, 253–5, 4 figs.

The Mikrosorban filter, made by a German firm, consists of synthetic fibres between 0·6 and 0·8 micron in diameter. It is readily soluble in benzene, tetralin and other organic solvents and is remarkably inert chemically. Drying at 40°C. removes water. The sole drawback is its low softening temperature due to the thermoplastic nature of the fibres.

Tests show the filtration efficiency to be 99·9% for a radioactive aerosol with all particles below 0·3 micron and 99·8% at 0·1 micron. An electrostatic effect is believed to contribute to this performance.

Against quartz dust up to 5 microns the efficiency was 99·8% and 500 mgm. could be collected on a filter 11 cm. in diameter without undue rise in resistance.

The resistance of a clean filter of this size was about 260 mm. water at 10 m.³/hour. *C. N. Davies*

HASSELT: INSTITUT D'HYGIÈNE DES MINES. Communication No. 161. Dosage de la silice dans les poussières de roches. 3e partie. Dosage de la silice libre par voie chimique dans les fines poussières. Mise au point d'un mode opératoire satisfaisant. **[The Silica Content of Rock Dust. Part 3. Chemical Estimation of Free Silica in Fine Dusts. Realization of a Satisfactory Method of Analysis]** [CARTIGNY, S.] 1959, May 15, v. 14, No. 4, 92 mimeographed pp., 16 figs. [37 refs.]

Having reviewed the various methods of determining free silica [see this *Bulletin*, 1958, v. 33, 1147] the author decided that the most promising were the process using pyrosulphate of potassium, due to TROSTEL and WYNNE, and the employment by HIRSCH and DAWIHL of pyrophosphoric acid as a solvent for silicates. The present report describes, in great detail, the study of the latter and its development into a simple, rapid and reproducible technique for examining fine dust from coal seams and a variety of rocks in samples containing 10–50 mgm. of mineral matter.

60 samples of quartz and 54 of silicate minerals, each having all, or nearly all, of its particles below 5 microns diameter, were prepared by sedimentation in water or air separation in a Zurlo classifier. They were sized visually under the microscope with an objective of 1·3 numerical aperture.

Preliminary experiments, which are fully described, led to the adoption of the following procedure. The sample is heated to 700°C. for half an hour in a specially designed electric furnace and thrown on the surface of 10 cc. of pyrophosphoric acid, the preparation of which is specified, in a platinum vessel. Heat is applied for 5 minutes on a special hot plate then for 10 minutes in a special electric muffle. The heating devices are designed to avoid local hot spots and to maintain a uniform temperature, aluminium block surrounds being incorporated for this purpose. Rapid cooling, dilution and filtration follow. The residue is then washed with hydrochloric acid and incinerated in the presence of sulphuric acid, first with a small flame, then in a furnace where it is dried at 850°C. and weighed. Finally it is treated with water, sulphuric and hydrofluoric acids and again evaporated and weighed. The difference between the weighings is the amount of free silica evaporated which, if the silicates have been completely dissolved away, is the free silica content of the sample subject only to correction for loss of free silica by solution during the separation.

It is shown that the loss of free silica is a linear function of the weight of the silica found in the sample and is inversely proportional, with some scatter, to the specific surface average diameter (determined from the count assuming lognormal distribution and the definition of HATCH and CHOATE). A basis for the solution correction is thus provided.

The procedure is tested on a number of mixtures of free silica with silicates and other substances and analyses are compared with results from other laboratories, including X-ray determinations. It is concluded that the proposed routine is satisfactory in all respects. *C. N. Davies*

CROSSMON, Germain. **The Value of Phase Microscopy for the Examination of Particulate Material collected on Membrane Filters.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 190–93, 6 figs.

Samples of dust, collected on millipore filters, are often examined microscopically by placing the filter, dust side down, on a slide and applying a drop of oil having the same refractive index as the filter which is thus rendered transparent. Unfortunately this very much decreases the light-field visibility of dusts such as quartz, diatomite and cristobalite which also have indices near to that of the clearing oil.

The effect is demonstrated by photomicrographs, illustrating the paper, which also show that the use of the phase contrast microscope overcomes the difficulty.

Complete removal of filter texture necessitates an oil of index 1·507 and it must have no solvent action upon the filter; suitable media are described. Practical points in the microscope set-up are discussed and an example is given of the use of polarizing equipment with the phase contrast microscope for the examination of birefringent particles. *C. N. Davies*

DIMMICK, R. L. **Jet Disperser for Compacted Powders in the One- to Ten-Micron Range.** *Arch. Indust. Health.* Chicago. 1959, July, v. 20, No. 1, 8–14, 2 figs.

After storage in a vacuum desiccator the powder to be dispersed as an aerosol is compressed into a cylindrical rod by the application of a screw in a closed tube. The rod of compressed powder may weigh 50 mgm. or more; 2,000 lb./in.² was found to be a suitable pressure for dry bacteria.

The rod is then driven by a manually operated screw against a system of jets fed with compressed air up to 20lb./in.² which successively erode the surface, subdivides the material removed and disperse it into the atmosphere.

Full descriptions are given of the compressing and dispersing devices.

The aerosol is generated in a rapid series of puffs so that a mixing chamber is needed to produce a more or less constant flow. Mass median diameters for the resulting clouds of particles are around 3 microns; the particles mostly carry a positive electric charge. Data are given for the recovery of viable organisms after dispersal. *C. N. Davies*

HOUBERECHTS, A. L'activité de l'Institut d'Hygiène des Mines au cours de l'année 1958. **[The Work of the Institut d'Hygiène des Mines during 1958]** Reprinted from *Ann. Mines Belgique.* 1959, No. 5, 47 pp., 36 figs. [67 refs.]

This annual report is familiar to readers of the *Bulletin* [for 1957 report, see this *Bulletin*, 1959, v. 34, 49]. It gives a summary of the work done during the year and of research in progress. During 1958 the special studies of the Medical Division included:

(1) Investigation of gas exchange in the lungs by means of the nitrogen meter.

(2) A study of the basic pathological lesions in pneumoconiosis in Belgian coalminers.
(3) Pharmacological action of acetylcholine and aleudrin [isoprenaline sulphate] in coalminers.
(4) Observations on physical and psychological effects of work at high temperatures during training of mine rescue teams.

The Engineering Division were again mainly concerned with the problems of dust control and physical environmental conditions underground.

A. Meiklejohn

CHARBONNAGES DE FRANCE. Compte Rendu des Journées Françaises de Pathologie Minière, Paris, 23–24 octobre 1958. [**Report of the French Conference on Mining Diseases, Paris, 1958**] 368 pp., illustrated. [Numerous refs.] 1959. Paris 8e: 9, Avenue Percier.

Since 1952 the Mining Industry in France has organized biennial conferences at which doctors, mining engineers and other experts, not only from France but from other countries, have met to discuss the problems of health in mines. The latest meeting was held in Paris on 23 and 24 October, 1958. The high regard in which these conferences are held is proved by the fact that the attendance had increased from 108 in 1952 to 293 in 1958, when the participants comprised 255 doctors (212 French and 43 from other countries) and 38 non-medical experts.

The programme was divided into 4 sessions covering:
(1) Accidents in coalmines;
(2) Progress in the control of environmental conditions in coalmines;
(3) Surgical treatment of tuberculosis complicating pneumoconiosis; and
(4) Recent advances in the pathogenesis of silicosis.

The first contribution from Dr. P. MAURIN (Lille) (*Psychosomatic aspects of accident-prone workmen. Rehabilitation of the disabled and related problems*, pp. 29–75) was based on the author's personal study of 536 accidents among miners; 305 (57%) were assessed as pure accidents and the remaining 231 (43%) as involving some contribution by the injured person. It is the latter group which is closely examined. Among the common contributory causes Maurin mentions endocrine disturbances of thyroid, suprarenal and sex glands; hypoglycaemia was occasionally observed; epilepsy and psychoses were rare. Synkinesis, that is involutary movements accompanying voluntary or reflex movements, was present in 17% of patients, usually associated with some degree of mental defect. Single accidents among these workmen tended to be unusually severe, indeed catastrophic; many suffered repeated accidents. Maurin agrees with experts in other countries that accident-prone persons have impaired psycho-motor function and suffer from anxiety due to domestic and social disturbances. He submits that an indispensable part of the investigation of these patients is to question the spouse about the patient's domestic and social behaviour, with particular reference to his attitude towards the children.

The contributions on rehabilitation of injured workmen were largely a recapitulation of accepted facts. Special comment was made on injuries involving the skull, spine and genital organs. In the discussion a note of warning was sounded on causalgia; the surgical treatment of painful parts by amputation, it was emphasized, often appeared dramatically successful but recurrence was frequent.

The session on the surgical treatment of tuberculosis opened with a film entitled: *Surgical removal of pulmonary tuberculous lesions in coalminers suffering from pneumoconiosis* (p. 155). The film (16 mm.) is in colour and runs for 30 minutes. It is obtainable on loan from Les Services des Relations publiques et sociales du Bassin Nord-Pas-de-Calais (20 rue des Minimes, Douai, Nord), and Les Charbonnages de France (9, avenue Percier, Paris, 8e).

P. RAZEMON, E. BALGAIRIES and P. NADIRAS contributed a paper on *The surgical removal of tuberculosis complicating pneumoconiosis among miners in the Bassin du Nord and Pas-de-Calais* (pp. 157–227). The earliest cases of silico-tuberculosis treated by surgical resection were operated upon because of mis-diagnosis. In some cases the massive radiographic shadows were regarded as cancer of the lung and in others as simple excavating tuberculosis. This experience, however, suggested that surgical treatment might be of value in some cases of pneumoconiosis accompanied by active tuberculosis particularly as the combined disease was invariably and rapidly fatal. Moreover, experience had shown that these patients did not benefit from chemotherapy, whereas those suffering from tuberculosis without pneumoconiosis did benefit.

The authors reported their experience of 110 patients whom they had treated surgically. In every instance meticulous care was taken to establish accurately the presence of both pneumoconiosis and tuberculosis.

The disease was identified as silicosis in 63 cases and as coalworkers' pneumoconiosis in 47; the presence of tubercle bacilli in the sputum was an essential criterion for diagnosis of tuberculosis. The suitability of patients for operation was based on careful radiological and pulmonary function studies. Pneumonectomy was performed in 4, lobectomy in 100 and segmental resection in 6 cases. The actual operation for the combined disease was considerably more difficult than for simple tuberculosis, owing to obliterative pleurisy, adhesions and enlargement of hilar glands. Deaths resulting from the operation or its complications amounted to 5 (4·54%) within 6 months. The results of follow-up are tabulated. Relative to the surgical treatment of tuberculosis accompanying pneumoconiosis the following matters are emphasized.

(1) Tuberculosis means sputum positive (tubercle bacilli +);
(2) Preliminary medical treatment should be maintained for 6 months, preferably in hospital or sanatorium;
(3) Tuberculous lesions should be confined to 1 lobe;
(4) Vital capacity should be at least 3 litres and MEV, 1 litre.

Cases of simple pneumoconiosis are more favourable than massive fibrosis for surgical treatment and best results are obtained in patients under 40 years of age.

A. MARMET and M. PETIT (*Surgical treatment of silicosis and tuberculous anthracosis*, pp. 229–251)

recorded their experience of 53 patients, 42 with coal-workers' pneumoconiosis and 11 with silicosis, treated surgically by them between 1952 and 1958. An interesting discussion followed and while there was general commendation of this advance in treatment, a feeling was expressed that the potentialities or limitations of chemotherapy in such cases had not yet been fully explored [this *Bulletin*, 1959, v. 34, 1262].

[Surgical treatment of tuberculosis complicating pneumoconiosis is still rarely practised in Great Britain. This contribution contains valuable guidance for chest physicians and thoracic surgeons. The publication of an English version is strongly recommended.]

The session on recent advances in the pathogenesis of silicosis was opened by E. VIGLIANI and B. PERNIS (Milan) followed by G. MOTTURA and F. LEVIS (Turin). Other contributions were made by research workers from France, Germany and Japan. [The whole of this work on the immunological hypothesis of the pathogenesis of silicosis has already been widely published in journals throughout the world and abstracted in this *Bulletin*.]

G. A. VOISIN (*Thoughts of an immunologist on the papers on the pathogenesis of silicosis*, pp. 343–348) outlined briefly the criteria necessary for attributing an immunological basis for a disease and described the nature of immunological reactions. He then examined the facts as they applied to silica and concluded by emphasizing the need to subject the hypothesis to careful laboratory research based on strict scientific conditions and controls.

[The immunological hypothesis has attracted great attention and the literature on it increases correspondingly. For most of us the subject is extremely abstruse. The urgent need is for an expert review and critical analysis by an immunologist or a report by a committee of enquiry.

This abstract would be incomplete without a tribute to the editors of the Report and to the quality of the production of the volume.] *A. Meiklejohn*

OCCUPATIONAL SAFETY & HEALTH. Geneva. 1959, Apr.-June, v. 9, No. 2, 63–9. **Meeting of Experts on the International Classification of Radiographs of the Pneumoconioses.** Geneva, 27 October to 7 November 1958.

In 1930 the experts attending the International Conference on silicosis at Johannesburg [this *Bulletin*, 1931, v. 6, 513] proposed an international classification of the pneumoconioses. The present development, however, derives from the Ninth International Conference on Industrial Medicine held in London in 1948 [*ibid.*, 1949, v. 24, 1023] where DAVIES and MANN described their researches into the classification of radiographs in coal-workers' pneumoconiosis in South Wales. Subsequently the ILO Conference at Sydney in 1950 [*ibid.*, 1954, v. 29, 626] recommended a classification of radiographs. This has since been extensively used in countries throughout the world with the notable exceptions of South Africa and U.S.A. The present meeting of experts at Geneva had the specific task of examining the results of the Sydney classification and making such modifications as seemed appropriate in order to overcome certain difficulties which had occurred. To facilitate the deliberations A. I. G. MCLAUGHLIN (United Kingdom) and V. VAN MECHELEN (Belgium) made a preliminary study and report on the working of the Sydney classification. Altogether they obtained the views of 120 experts from 16 countries. In preparing the revised classification which is reproduced the following matters were stressed:

(1) The diagnosis of pneumoconiosis must be based on the occupational history, clinical, radiographic and other appropriate investigations;
(2) The difficulty of using a single classification for the radiographic appearances of all the pneumoconioses provoked by mineral dusts;
(3) The classification is based on "persistent" opacities and excludes transient opacities.

"Object of The Classification"

"The object of the classification was to codify the radiological appearances of the pneumoconioses in a simple reproducible way. This would enable statistical and epidemiological investigations to be undertaken to assess the size and nature of pneumoconiosis problems and determine the steps to be taken for the control of the disease. The classification was not intended to define pathological entities, nor to take into account the question of working capacity. In particular, it would have no relation to the legal definition of stages of pneumoconiosis for compensation."

"Definition"

"At the end of the general discussion, the experts adopted a definition for the classification as follows:

'International classification of persistent radiological opacities in the lung fields provoked by the inhalation of mineral dusts.'

They intended that this definition should cover all coal and carbon dusts."

3 main groups of opacities are recognized: linear opacities, small opacities and large opacities [there is a conflict of terminology here but presumably small and large signify circular opacities]. The introduction of linear opacities is new and from the exchange of opinions it appears that it was not generally acceptable. The members, however, agreed to accept the innovation on a trial basis for industries with a high silica risk. It was underlined that it would *not* apply to coalminers. Small opacities (formerly simple pneumoconiosis) are again divided into categories 1, 2 and 3 and the size of the opacity is denoted by:

p = punctiform—previously pinhead.
m = micro-nodular or miliary—*not* to be used for mixed.
n = nodular.

Large opacities are divided into A, B and C; the previous category D was considered descriptively anomalous and so was eliminated. Complications or abnormalities are recorded by symbols of 2 letters, for example (tb) opacities suggestive of tuberculosis; (em) marked emphysema. [The classification is here reproduced in full for the convenience of readers.]

INTERNATIONAL CLASSIFICATION OF PERSISTENT RADIOLOGICAL OPACITIES IN THE LUNG FIELDS PROVOKED BY THE INHALATION OF MINERAL DUSTS [1]

(Geneva, 1958)

	No pneumoconiosis	SUSPECT	PNEUMOCONIOSIS											
Type of opacity			Linear opacities	Small opacities									Large opacities		
Qualitative features	O	Z	L	p			m			n			A	B	C
Quantitative features				1	2	3	1	2	3	1	2	3			
Additional symbols	(co)/(cp)	(cv)	(di)	(em)			(hi)			(pl)			(px)		(tb)

[1] Including coal and carbon dusts.

DEFINITIONS AND COMMENTS

The object of the classification is to codify the radiological appearances of the pneumoconioses in a simple, easily reproducible way. It is intended to describe the radiographic appearances of the persistent opacities associated with pneumoconiosis, not to define pathological entities, nor to take into account the question of working capacity.

Where there is an appreciable difference in the appearance of the two lungs, the two appearances may be described separately, beginning with the right lung.

No pneumoconiosis	O	No radiographic evidence of pneumoconiosis.
Suspect opacities	Z	Increased lung markings.

Pneumoconiosis

Linear opacities	L	Numerous linear or reticular opacities, the lung pattern being normal, accentuated or obscured.	
Small opacities [1]		*The following types are defined according to the greatest diameter of the predominant opacities.*	*The categorization depends on the extent and the profusion of the opacities.*
	p	Punctiform opacities. Size up to 1·5 mm.	*Category 1:* A small number of opacities in an area equivalent to at least two anterior rib spaces and at the most not greater than one-third of the two lung fields.
	m	Micro-nodular or miliary opacities. Greatest diameter between 1·5 and 3 mm.	*Category 2:* Opacities more numerous and diffuse than in category 1 and distributed over most of the lung fields.
	n	Nodular opacities. Size between 3 and 10 mm.	*Category 3:* Very numerous profuse opacities covering the whole or nearly the whole of the lung fields.
Large opacities [2]	A	An opacity having a longest diameter of between 1 and 5 cm, or several opacities each greater than 1 cm, the sum of whose longest diameters does not exceed 5 cm.	
	B	One or more opacities, larger or more numerous than those in category A, whose combined area does not exceed one-third of one lung field.	
	C	One or more large opacities, whose combined area exceeds one-third of one lung field.	

Additional symbols

Recommended additional symbols [3]	(co)	abnormalities of the cardiac outline. To be replaced by (cp): cor pulmonale, if this condition is strongly suspected.
	(cv)	cavity.
	(di)	significant distortion of the intra-thoracic organs.
	(em)	marked emphysema.
	(hi)	marked abnormalities of the hilar shadows.
	(pl)	significant pleural abnormalities.
	(px)	pneumothorax.
	(tb)	opacities suggestive of active tuberculosis.

[1] The choice of order of the symbols is left to the convenience of the physician.
[2] The background of small opacities should be specified as far as possible
[3] The use of these symbols is optional.

As verbal descriptions were considered to be inadequate sets of standard reference films are to be prepared for distribution. Standards of radiographic technique are set out.

It was acknowledged that miniature radiographs (photofluorography) cannot be relied upon for accurate diagnosis especially in the early stages of the disease. This notwithstanding 70 x 70 mm. films are extensively used in many countries as an inexpensive means of periodical radiographic examination. The experts recommend that the new classification should be used in trials scientifically devised to compare its value for use with large and miniature films.

[The value of a satisfactory International Classification —if it can be devised—cannot reasonably be disputed. Many will have personal objections to the new code but it is to be hoped that experts in all countries will test it objectively and record their experience and offer constructive criticism. For reference purposes the classification should have a short title such as "Geneva Classification, 1958". The meeting refers to berylliosis as a pneumoconiosis; is this valid? In Great Britain under the National Insurance (Industrial Injuries) Act poisoning by beryllium or a compound of beryllium is listed as a specific Prescribed Disease.] *A. Meiklejohn*

Brina, A., Rubini, G. & Racca, G. Studio vettorcardiografico del cuore nella silicosi. [**Vectocardiographic Study of the Heart in Silicosis**] *Med. d. Lavoro.* 1959, June–July, v. 50, Nos. 6/7, 432–6. [Numerous refs.]

The English summary appended to the paper is as follows:—

"36 cases of silicosis were studied with a vectocardiographic technique both at rest and during muscular work. Parallel electrocardiographic studies were made. The results were the following: vectocardiographic examinations showed lesions in the right cavities in 25 cases both at work and rest; electrocardiographic examinations revealed pathological changes only in 14 cases both at work and at rest. We can conclude that vectocardiography is a more sensitive technique than electrocardiography in detecting early lesions of the right heart."

Brina, A., Agnoletto, A. & Villa, A. Indagine fonocardiografica durante manovra di Azoulay in soggetti normali e in pneumopatici cronici. [**Phonocardiographic Investigation during Azoulay's Test in Normal Subjects and in Chronic Pneumopathies**] *Med. d. Lavoro.* 1959, June–July, v. 50, Nos. 6/7, 437–40. [12 refs.]

The English summary appended to the paper is as follows:—

"31 patients with silicosis and 10 with asthmatic bronchitis were studied by means of phonocardiography during Azoulay's test. About 2/3 of the observed cases showed some changes in the acoustic findings at rest, namely: 1) increase, for several minutes, of the pre-existing reinforcement or splitting of the pulmonary second sound or of puff; 2) appearance of a gallop rhythm, considering how scarce acoustic findings are in patients with chronic lung diseases, the phonocardiographic tracing during Azoulay's test seems to be of some use for diagnostic purposes, in view of its simplicity and of the obtained results."

Brina, A., Ghia, C. & Racca, G. Studio oscillografico di pneumopatici cronici mediante prova di Valsalva-Flak. [**Oscillographic Study of Chronic Pneumopathic Patients by means of Valsalva-Flak's Test**] *Med. d. Lavoro.* 1959, June–July, v. 50, Nos. 6/7, 441–6, 1 fig.

The English summary appended to the paper is as follows:—

"Endothoracic pressure variations induce some peripheral circulation changes that can be detected through oscillography. The Valsalva-Flak test was performed by a group of pneumopathic patients including 21 silicotic patients. Performing the test induces a more or less marked reduction of the oscillographic index in patients with chronic bronchitis and emphysema and in patients with asthmatic bronchitis, as well as in normal subjects, while the typical flattening of the curve is lacking in cases of confluent and massive silicosis. It is suggested that the cause of these findings is the stiffness of lung parenchyma in subjects with diffuse confluent silicosis."

Buscarini, L. & Nicrosini, F. Le sieroproteine e le sieroglicoproteine nella silicosi polmonare. [**The Proteins and Glycoproteins in the Blood Serum of Patients with Silicosis**] [*Med. d. Lavoro.* 1959, May, v. 50, No. 5, 368–78, 4 figs. (2 on 2 pls.). [Numerous refs.] English summary.

These authors report a study of 29 cases of silicosis among workmen in a Pavia pottery. Radiologically, 9 patients were at Stage I (diffuse interstitial sclerosis), 5 were at Stage II (nodular dissemination) and the remaining 15 were at Stage III (pseudotumour formation). They first estimated the proteins and glycoproteins in 30 normal subjects aged 18–42 years and so established normal averages, with standard variations, for total proteins, the various globulins and certain carbohydrate groups of the glycoproteins, and they then carried out similar estimates on specimens of blood serum from the 29 patients in their series.

In all the cases of silicosis the investigation showed a constant rise in serum proteins which was largely due to alpha and gamma globulins. The serum albumins were somewhat low but within the normal range. The rise in proteins and alpha globulins was more marked at Stage III of the disease but the rise in gamma globulins was more or less similar in all 3 groups. The authors found a progressive increase, with the stage of the disease, of the carbohydrate groups which were combined with protein compounds to form the glycoproteins of the serum.

An account is given of the technique followed in these investigations.

The authors conclude that the measurement of the proteins and more particularly the glycoproteins in the blood serum of patients with silicosis provides useful information as to the stage of development of the disease. *J. Cauchi*

VIGLIANI, E. C. Criteri di orientamento sulle cosiddette "massime concentrazione biologiche tollerabili." [**Criteria on the So-Called "Maximum Biological Allowable Concentrations"**] *Med. d. Lavoro.* 1959, May, v. 50, No. 5, 323–7. English summary.

The adoption of a tolerance limit or ceiling for an industrial poison presumes that the toxic substance is absorbed, and excreted in due course, by the exposed worker or that it accumulates in his body; for substances which are excreted in the expired air or in the faeces directly after absorption no tolerance limits need be laid down.

The necessary measurements may be of (a) the toxic element or substance itself, or (b) substances which derive from its metabolism in the body, or (c) other substances which are formed in the body as a result of the toxic action. In most cases the samples to be examined are of blood or urine; in other cases the expired air or skin appendages such as hair are tested. With radioactive substances it may be possible to assess total contents for the whole body or for the "critical" organ.

In the case of certain industrial poisons no single figure can be laid down as maximum tolerance concentration. Some heavy metals and other substances concerned with industrial poisoning may already be present in the body under normal conditions in quantities which vary with the environment. With some individuals the rate of excretion may fluctuate within the 24 hours and the sample to be examined may have to be taken from the pooled output of 24 hours or even of several days.

The testing of biological samples for the concentration of an industrial poison or its derivatives may, under certain circumstances, provide an indirect method of assessing the concentration of the poison in the works environment. *J. Cauchi*

Substance	Estimated as	Maximum Allowable Concentration	Biological Material
Lead	lead	0·15 mgm./litre	urine
„	„	0·08 „	blood
„	coproporphyrin	0·10 „	urine
Tetraethyl lead	lead	0·12 „	„
„ „	„	0·07 „	blood
Mercury	mercury	0·10 „	urine
Chromium	chromium	0·04 „	„
Arsenic	arsenic	0·10 „	„
„	„	3 μgm./gm.	hair
Benzol	conjugated sulphates	70%	urine
Trichloroethylene	trichloracetic acid	50 mgm./litre	„
Acetone	acetone	50 „	blood
„	„	100 „	urine
„	„	0·12 „	expired air
Toluol	hippuric acid	2·4 gm./24 hours	urine
Parathion	cholinesterase activity	reduced by 5%	blood
CO	COHb	14%	„
„	CO	3cc.%	„
„	„	0·014%	expired air
HF	fluoride	2 mgm./litre	urine

PARMEGGIANI, L. Orientamenti predominanti in Italia in tema di massime concentrazioni tollerabili dei tossici nelle industrie. [**Prevailing Opinions in Italy on the Problem of Maximum Allowable Concentrations**] *Med. d. Lavoro.* 1959, May, v. 50, No. 5, 328–31. [29 refs.]

Meeting in 1956, the American Conference of Governmental Industrial Hygienists defined "maximum tolerance concentrations of industrial poisons" to be the highest concentration of each poison in the atmosphere which the workman at risk can inhale without prejudice to his health working an 8-hour day, 6 days a week, in a working lifetime. The harmfulness of an industrial poison may be due to toxicity or carcinogenicity, or the poison may have an irritant or an asphyxiating action.

The limits of concentration adopted for any industrial poison must be such as will protect new entrants as well as those who have developed some tolerance after a period of repeated exposure. With the heavy metals and some other industrial poisons, cumulative action must be taken into account.

The progress already made in the prevention of industrial poisoning through control of the working environment will be enhanced when, as it is hoped, standards of maximum tolerance concentrations are adopted by international agreement. *J. Cauchi*

PINIZZOTTO, G. A proposito di un caso di artropatia saturnina. [**Saturnine Arthropathy**] *Rass. Med. Indust.* Rome. 1959, Jan.–Feb., v. 28, No. 1, 1–10, 3 figs. [12 refs.] English summary (8 lines).

A man aged 47 had worked for 36 years painting designs with lead paint on ceramic products. Although he gave a long history of vague illness with asthenia, abdominal pain, etc., the present symptoms began 1 year previously with especially increased abdominal pain, marked asthenia, and "claw" hand. On examination

there was a definite blue line on the gums, pallor, pain on abdominal palpation, enlarged liver and marked deformation of the finger joints particularly the proximal joints, ability to extend them was almost absent the hands being held in the "claw" position. Laboratory examination showed albuminuria and marked porphyrinuria with deficient urinary concentration, no basophilia; X-ray showed chronic enterocolitis and gastritis, and definite arthropathy of the fingers most marked on the right side.

When he was too young to remember it, the patient had had a severe thoracic operation which had left a marked scoliosis and fusion of the left 5th, 6th, and 7th ribs with retraction of the lung.

The author points out that although cases of this saturnine gouty arthropathy may be rare, only occurring after long exposure (15–20 years after commencing intoxication), in completely unsatisfactory hygienic conditions, the condition does call attention to the need for proper preventive measures even in the smallest establishments. *W. K. Dunscombe*

PERNIS, B. & BAIRATI, A., Jr. Il midollo osseo nel saturnismo al microscopio elettronico. **[Electron Microscope Study of Bone Marrow in Saturnism]** *Med. d. Lavoro.* 1959, June–July, v. 50, Nos. 6/7, 447–57, 8 figs.

The English summary appended to the paper is as follows:—

"The authors have studied with the electron microscope ultra-thin sections of sternal bone marrow of two patients with patent lead poisoning. In both cases many marrow erythrocytes and erythroblasts showed submicroscopic alterations consisting in swelling and disorganisation of mitochondria. In some cells the mitochondria were filled with ferritin granules.

"These alterations, comparable with those previously observed in the red blood cells of lead-poisoned guinea pigs, are likewise interpreted as due to lead-induced disturbances of heme synthesis, many steps of which take place in the mitochondria."

JHAVERI, S. S. **A Case of Cirrhosis and Primary Carcinoma of the Liver in Chronic Industrial Arsenical Intoxication.** [Miscellanea] *Brit. J. Indust. Med.* 1959, July, v. 16, No. 3, 248–50. [12 refs.]

This is a detailed case report of a man who had handled arsenious oxide and sodium arsenate for more than 20 years and who died at the age of 53, 7 years after his first admission to hospital for ascites. Protective masks and gloves were usually worn. Alcohol consumption was small. At that time a 24-hour specimen of urine contained 0·13 mgm. of arsenious oxide, equivalent to 0·86 p.p.m. He returned to his work and remained well for 5 years until February 1956 when his terminal illness began. Laparotomy showed thickened parietal peritoneum, adherent bowel and cirrhosis of the liver. He did not return to work and was readmitted in October 1957 and died a fortnight later. The skin was typical of chronic arsenical poisoning but arsenic was not detected on biopsy. The hair, weighing 0·1379 gm., contained 209 p.p.m. of arsenious oxide and nail clippings, weighing 0·039 gm., contained 564 p.p.m., figures much higher than those published for workers in the arsenic industry. In a full post-mortem report it is shown that the liver weighed 1,400 gm., there was very little remaining liver tissue, its place being taken by nodules of carcinoma, and any liver tissue seen was fibrous. The cause of death was haemorrhage from oesophageal varices and primary carcinoma of the liver with plastic peritonitis. The clinical picture and the positive laboratory findings indicated chronic arsenical poisoning and in the absence of other aetiological factors arsenic appeared to have been the cause of the cirrhosis-carcinoma.

After outlining the 3 forms of industrial arsenical poisoning, the author points out that the hepatotoxic action of inorganic arsenic compounds has long been recognized when they are used therapeutically but it has scarcely been mentioned as an industrial hazard.

M. Patricia Fitzsimons

BARTALINI, E. Studio sperimentale sulla tossicità di un composto organico dello stagno usato come plastificante. **[Experimental Study of the Toxicity of a Tin Organic Compound used as a Plastifier]** *Med. d. Lavoro.* 1959, May, v. 50, No. 5, 338–50, 3 figs. [Numerous refs.] English summary.

A firm wished to use certain organic compounds of tin (dibutyl tin oxide) as plastifiers of recently synthetized polivinyl resins in the manufacture of toys and household ware and asked the author first to examine the ingredient and proposed products for possible toxicity.

Rats were fed, some with high doses and others with smaller doses over longer periods, to investigate both acute poisoning and also any cumulative action and chronic poisoning. The author studied the solubility of the proposed plastifier in artificially prepared "saliva" and "gastric juice" and inserted grafts of the plastic—subcutaneously, intramuscularly and intraperitoneally—into rabbits which were killed after a period for post-mortem examination. The grafts produced no inflammatory reactions in the rabbit tissues. After ingesting daily 100 mgm./kgm. of dibutyl tin oxide the rats were ill by the second or third day and died by the fifth day; post-mortem examination showed degenerative changes in the liver and kidneys. After daily doses of 25 mgm./kgm. the rats were dead within 11 days with similar symptoms and post-mortem findings. Other rats were given daily doses of 2·5 mgm./kgm. of the plastifier for 60 days and then killed though apparently in good health; their liver and kidneys showed some slight changes with signs which were suggestive of recovery.

Using a spectrographic technique, the author demonstrated the presence of tin in the liver and kidneys of these rats. He also examined the spleen of the rats which had received the lower and longer dosing but he failed to demonstrate any tin in this organ.

On the basis of his findings, the author considers that dibutyl tin oxide is too toxic and too soluble in saliva and in gastric juice for its use as a plastifier to be safe.

J. Cauchi

CLARK, Janet H. **The Denaturation of Proteins by Chromium Salts.** *Arch. Indust. Health.* Chicago. 1959, Aug., v. 20, No. 2, 117–23, 3 figs.

In vitro experiments showed that bovine blood plasma albumin was denatured by both trivalent and hexavalent compounds at *p*H less than 5·4 (*i.e.* the isoionic point of the protein). The rate of denaturation was slow at low temperatures but proceeded rapidly at temperatures between 35° and 40°C. Essentially similar results were obtained with crystalline egg albumin. The experiments suggest that denaturation of proteins by chromium compounds may occur *in vivo* for those proteins with isoelectric points near *p*H 7·0. *Richard Doll*

BAETJER, A. M., LOWNEY, J. F., STEFFEE, H. & BUDACZ, V. **Effect of Chromium on Incidence of Lung Tumors in Mice and Rats.** *Arch. Indust. Health.* Chicago. 1959, Aug., v. 20, No. 2, 124–35. [22 refs.]

The incidence of lung cancer is known to have been high in certain chromate manufacturing plants in Britain, Germany and the U.S.A., but it is not known what substance was responsible for the disease. Experiments were, therefore, undertaken in which mice were exposed to a mixed chromium dust, similar in composition to the dust which had been in the air of the plants, by inhalation in a dust chamber, by intratracheal injection or by intrapleural injection. Other mice were exposed to zinc chromate or to barium chromate by intratracheal injection or by intravenous injection. Altogether 1,347 mice were exposed to chromium compounds and 1,321 mice were observed as controls. In addition 150 rats were exposed to the mixed chromate dust in a dust chamber or by intratracheal injection and 142 rats were observed as controls.

No true bronchogenic carcinomas were observed in either rats or mice and no clear excess of any type of malignant growth was observed among the treated animals. The difference between these negative results and the positive results reported by HUEPER with intrapleural injections in rats [this *Bulletin*, 1959, v. 34, 138] may be due to a species difference in reactivity.

Richard Doll

ARCH. INDUST. HEALTH Chicago. 1959, Sept., v. 20, No. 3, 266–70. **Threshold Limit Values for 1959. Adopted at the 21st Annual Meeting of the American Conference of Governmental Industrial Hygienists** [COLEMAN, A. L., Chairman.] Chicago, April 25–28, 1959.

BAETJER, A. M., DAMRON, C. & BUDACZ, V. **The Distribution and Retention of Chromium in Men and Animals.** *Arch. Indust. Health.* Chicago. 1959, Aug., v. 20, No. 2, 136–50, 3 figs. [20 refs.]

Experiments were undertaken to determine the mechanism by which chromium compounds could produce bronchogenic cancer. Analysis of lung tissue from men who had worked in a chromate producing plant showed that both soluble and insoluble chromium were present in the lung tissues many years after the exposure to chromates had ceased. The soluble chromium was bound by cellular tissue and was insoluble in saline, acetone and dilute base but was readily soluble in concentrated acid. For neither type of chromium did the concentration appear to be related to the presence or absence of cancer.

Lung slices bound chromate to a greater extent and more rapidly when in contact with chromic ions than when in contact with chromate or dichromate ions. Human, rat and guineapig slices appeared to bind chromium to a similar extent. After intratracheal injection into animals water-soluble sodium chromate or potassium dichromate was removed from the lungs within a few days, but traces remained for at least 140 days. Some of the chromium was excreted, some was distributed in the soft tissues, but a large part was taken up by the red cells and was subsequently deposited in the spleen. The water-soluble hexavalent and trivalent chromium retained by the tissues was retained in a form insoluble in saline extracts.

Water-soluble chromic chloride, when injected into animals, remained to a large extent and for long periods locally at the site of injection. Some was distributed in the plasma and was removed by the spleen.

Richard Doll

HUEPER, W. C. & PAYNE, W. W. **Experimental Cancers in Rats produced by Chromium Compounds and their Significance to Industry and Public Health.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug., v. 20, No. 4, 274–80, 8 figs. [14 refs.]

Previous experiments showed that the implantation of powdered chromite ore roast in sheep fat into the soft tissues of the thigh or intrapleurally in rats was followed in a small proportion of instances by the development of carcinoma or sarcoma. In the present series of experiments pellets of 25 mgm. of a pure chromium compound and 50 mgm. of sheep fat were tested in a similar way. The compounds used were calcium chromate, sintered calcium chromate, sintered chromium trioxide and barium chromate; *i.e.* hexavalent chromium compounds and mixtures in which some of the chromium was reduced to lower valences. Each material was tested by each method of injection on batches of 20 male and 15 female rats. Within 12 months many tumours had developed; tumours were present in 29 of the 70 rats which had been given calcium chromate, in 25 of the rats given sintered calcium chromate, in 29 of the rats given sintered chromium trioxide, but in none of the rats given barium chromate or sheep fat alone. The effect of the different chromium compounds was approximately proportional to their solubility in water.

Richard Doll

BRESLIN, A. J. & HARRIS, W. B. **Health Protection in Beryllium Facilities. Summary of Ten Years of Experience.** *Arch. Indust. Health.* Chicago. 1959, June, v. 19, No. 6, 596–648, 29 figs. [Numerous refs.]

This long paper describes the extensive experience of the United States Atomic Energy Commision in handling

beryllium over the past 10 years, *i.e.* the period after which most cases of beryllium disease occurred.

It gives details of the extent to which the various maximum allowable concentrations of beryllium, recommended in 1948, may be temporarily exceeded in and around Atomic Energy Commission Plants.

Problems within the plant, of process design, exhaust ventilation, operating procedures, housekeeping, and personal protection, are described and illustrated in detail. So too are problems outside the plant, such as estimating and measuring stack effluents, selecting air cleaning equipment and disposing of waste. The programme for training staff, monitoring the air, both in and out of the plant, and medical supervision, is described.

7 tables are given, showing maximum, minimum, and median concentrations of beryllium, found around various common beryllium handling operations. These data are then grouped into average exposures, and attempts are made to relate these to the occurrence of disease. Sympathy with the difficulty of this operation is more easily evoked than conviction by its results. However, one very practical conclusion is reached: "there is probably no way to sample adequately the actual exposure of new personnel involved in breaking in new untried equipment". It is at such times that disease may occur.

In the light of all the remaining uncertainties about the relationship of exposure to disease we may perhaps be glad, that, "in view of the public attitude, the treatment of wastes in some cases requires greater care than indicated by the potential hazard".

There is an appendix, giving details of chemical, spectrographic, and fluorimetric methods of air analysis, and a bibliography. *C. H. Wood*

FUCHS, A., PALECKOVÁ, B. & BARTONOVÁ, M. Riziko benzenu při práci s lepidly na kůží. [**The Hazard of Benzene in Work with Glues for Leather**] *Českoslov. Hyg.* Prague. 1959, v. 4, No. 8, 437–45, 3 graphs. [26 refs.]

The English summary appended to the paper is as follows:—

"In two workshops where rubber glue with a small amount of benzene—not more than 6%—is used, measurements of the concentration of benzene in air have been carried out. At the same time benzene and phenol as its metabolite have been determined in urine of the workers. The average concentrations of benzene in air are in good agreement with the average concentrations of phenol in urine. The determination of benzene in urine is of little value for the sanitary inspector as it offers only qualitative information, and as we have tried to show, not always even that. The question, if the obtained values of benzene in air which are higher than the maximum permissible concentrations mean a health hazard or not is to be discussed later. Finally, some arrangements have been suggested, which might lower the health hazards even in the present conditions and criteria have been discussed when the glues with the amount of benzene higher than 6% might be used, or what kind of glue could replace them."

GUERTIN, D. L. & GERARDE, H. W. **Toxicological Studies on Hydrocarbons. IV. A Method for the Quantitative Determination of Benzene and Certain Alkylbenzenes in Blood.** *Arch. Indust. Health.* Chicago. 1959, Sept., v. 20, No. 3, 262–5, 2 figs.

"An ultraviolet spectrophotometric method has been described for the quantitative determination of benzene and alkylbenzenes in blood. The procedure involves hemolysis of the sample and subsequent extraction of the hydrocarbon with cyclohexane. The ultraviolet absorption spectrum of the cyclohexane solution is recorded, and the concentration of aromatic is determined by reference to previously prepared calibration curves. The method has been applied to the determination of a number of alkylbenzenes and kerosene, used in a systematic study of the rates of absorption and elimination of these types of hydrocarbons from the blood stream of experimental animals. This work will be described in a future publication."

TROMPEO, G. Rilievi sull'inquinamento ambientale da tricloroetilene nelle piccole lavanderie a secco. [**Observations on Environment Pollution from Trichloroethylene in Small Dry-Cleaning Shops**] *Igiene Moderna.* 1959, Jan.–Feb., v. 52, Nos. 1/2, 112–26, 5 figs. [48 refs.] English summary (9 lines).

The plant was used between 3 and 8 times daily, the cleaning solvent in 15 shops being trichloroethylene and in 5 perchlorethylene. Air samples were collected throughout the week before and after work each morning and afternoon, near the drum and at the point farthest away and also where the ironing was done. 120 atmospheric concentrations shown in a table range from 0·025 to 2 mgm. per litre of trichloroethylene and from 0·025 to 0·35 of perchlorethylene.

Before the drum was opened samples were also collected during its operating phases: trichloroethylene permeation of the contained materials; centrifugal removal of liquid by quickening the revolutions; removal of vapour by compressed warm air; exhaustion of vapour by reversing the flow. A cumulative increase in concentrations during successive operations was most marked during each 3rd phase. The mid-day break resulted in better clearing of the lower concentrations found in shops with cross ventilation than in 8 without. Where the amount of work was small, end of the day concentrations of 0·3 mgm. per litre were the same as at mid-day; where it was large they were 0·65 and 0·6 mgm. per litre respectively, this because the cleaned materials obstructed ventilation and also because solvent residues evaporated from them. New machines gave median air concentrations of 0·4 mgm. per litre, older ones double this, and the newest, those using perchlorethylene, less than half. In 12 shops the worker was exposed to more than 0·55 mgm. per litre for at least 6 hours daily, and in 4 to more than 1 mgm. per litre trichloroethylene.

Signs of absorption, not enough for poisoning, in a few of the workers are being investigated.

The machines, though closed, would be better encased, cleaned materials should remain in cupboards and both should have downward exhaust ventilation.

M. Patricia Fitzsimons

KASBEKAR, D. K., LAVATE, W. V., REGE, D. V. & SREENIVASAN, A. **A Study of Vitamin B_{12} Protection in Experimental Liver Injury to the Rat by Carbon Tetrachloride.** *Biochem. J.* 1959, July, v. 72, No. 3, 384–9. [41 refs.]

This paper on estimations of several metabolites in homogenized liver fractions, including centrifugally separated cell fractions of nuclei and mitochondria, was submitted early in 1958 by the Department of Chemical Technology of the University of Bombay. In the same journal an account of similar investigations in experimental thyrotoxicosis appears first.

The early temporary changes following carbon tetrachloride intraperitoneally—loss of vitamin B12 from the liver and particulate fractions of the cells and depletion of soluble sulphydryl compounds from the supernatant fraction—probably provoked the degenerative processes in the liver. Later there was depletion of liver ribonucleic acid, phospholipids, glycogen and protein and an accumulation of fat. Except for glycogen depletion, which was still pronounced after 48 hours, intraperitoneal administration of 10 μgm. vitamin B12 3 hours before poisoning prevented or counteracted the metabolic disturbances. Methionine levels were unaffected in both groups.

Mitochondria in the experiments with thyrotoxic rats were affected also and the vitamin protection mechanism was similar in these apparently unrelated metabolic stress conditions. The phenomenon of vitamin B12 protection is non specific and may be due to an effect on mitochondrial integrity. *M. Patricia Fitzsimons*

ROCKHOLD, W. T., WRIGHT, P. G. & STOKINGER, H. E. **The Toxicity of Methyl Divinyl Acetylene.** *Arch. Indust. Health.* Chicago. 1959, Aug., v. 20, No. 2, 151–4, 1 fig.

This newly synthesized compound, 2-methyl-1,5-hexadiene-3-yne, was available for acute toxicity studies. It is a colourless liquid, insoluble in water; mol. wt. 92; SG 0·785; MP −65°F.; BP 226°F. Details are given of an infra-red spectrogram but it revealed no characteristics which could be used for analysis of atmosphere exposure or body fluids.

In rats the calculated LD50 was greater than 3·2 gm. per kgm. orally. The 30-day LD50 intraperitoneally was 2 gm. per kgm., and slight central depression was noticed; double this dose caused immediate slowing of respiration and prostration within 10 minutes, 1 death occurring within 45 minutes, 2 others on the same day and the last on the 30th.

In rabbits, single applications of 0·01 ml. to the clipped skin produced questionable erythema, not visible next day; applications to the same area of 0·25 ml. 3 times daily at 3-hour intervals for 3 days caused moderate erythema after the first day which did not increase and it subsided 2 days afterwards leaving some scale-like sloughing. There were no systemic effects at the time or during 4 months' observation. Fluorescein tests showed no irritative or other ocular damage after instillation of the maximum tested dose of 0·25 ml. of methyl divinyl acetylene.

In rats pilot inhalation exposures for 2 hours daily to 500 p.p.m. for 7 days and to 900 for 4 were not lethal or toxic. Inhalation of "substantially saturated" vapour for 1 hour produced anaesthesia within 30 minutes but normal recovery occurred without toxic effect 1 hour after removal. In comparison, methyl acetylene at concentrations of 28,700 p.p.m. for 6 hours daily on 5 days a week for 6 months produced only some degree of pulmonary irritation.

The results indicate that methyl divinyl acetylene is a "slightly toxic" compound which has a safety margin between narcotizing and fatal concentrations.

M. Patricia Fitzsimons

KILLICK, Esther M. & MARCHANT, Jean V. **Resuscitation of Dogs from Severe Acute Carbon Monoxide Poisoning.** *J. Physiology.* 1959, Sept. 2, v. 147, No. 2, 274–98, 4 figs. [34 refs.]

In this investigation 59 dogs were exposed in boxes to mixtures of CO in air varying from 0·187 to 0·356% CO. Exposures varied from 34 to 101 minutes depending upon the time taken for the animal to become deeply unconscious and to verge on respiratory failure as judged by slowing respiration and diminished inflow of oxygen to the box.

The commonest first sign of poisoning was unsteadiness or stiffness in the legs—the dog often fell. Usually within 10–20 minutes there was a marked increase in respiration, but the breathing rate dropped again in many animals after 30 minutes. When the dog lay down, it became drowsy and slowly lapsed into unconsciousness. The onset of symptoms varied with concentration of CO, with activity and with frequency of respiration.

4 dogs were dead when removed from the box, arterial blood taken *post mortem* showing 86, 78, 81·2, and 87·5% of the haemoglobin combined with CO. A 5th died after breathing 0·24% CO in air through a mask; blood at autopsy showed that 77·5% of the haemoglobin was combined with CO. 3 dogs died within 2 minutes of removal from the box (72, 72·5, and 76·5% haemoglobin combined with CO), 1 dog breathed 5% CO_2 + 95% O_2 for 11 minutes and died with only 41% of the haemoglobin combined with CO and another died after breathing this mixture for 5 minutes. The remaining 49 dogs survived. 9 were resuscitated by breathing air, 20 by breathing 100% oxygen and 20 by breathing 5% CO_2 + 95% O_2.

The rate of disappearance of CO from the blood was faster in those dogs resuscitated by breathing pure oxygen than in those breathing air, and faster again in those breathing 5% CO_2 + 95% O_2 than in those breathing pure oxygen. During the first hour more CO disappeared from the blood than was recovered in the expired air, in all 3 groups, though a greater proportion was recovered in the 5% CO_2 group than in the other 2. There is much interesting discussion and statistical detail

concerning the blood analysis of individual dogs in this paper.

The clinical recovery of those dogs breathing 100% O_2 was markedly faster on the whole than in those breathing air. The difference between those breathing pure oxygen and the CO_2 mixture was small, but complete recovery tended to occur earlier in the CO_2 group. Subsequent sequelae were few and incidence about similar in the 3 groups.

This paper makes a valuable contribution to the controversy as to whether oxygen or a mixture of oxygen and CO_2 should be used for resuscitating those poisoned from CO, since the blood of dogs has relative affinities for O_2 and CO very close to those of human blood. It provides no evidence, however, for the less important debate as to whether a 7% mixture of CO_2 is more effective than a 5% mixture (*Brit. Med. J.*, 1958, Dec. 6, 1408; Dec. 27, 1591) [see also this *Bulletin*, 1959, v. 34, 1142]. *T. O. Garland*

ZAMBRANO, A. Cinque infortuni mortali da composti fosfo-organici in agricoltura. [**Five Mortal Accidents from Organic Phosphorus Compounds in Agriculture**] *Rass. Med. Indust.* Rome. 1959, Jan.–Feb., v. 28, No. 1, 36–49. [32 refs.] English summary (5 lines).

After emphasizing the grave risk to which agricultural workers are exposed when working with organic phosphorus compounds, the author points out that in Italy because of the large number of very small farms and family holdings it is extremely difficult to get information as to the dangers of these products to the workers and to carry out preventive measures.

The most generally used product contains varying amounts of parathion; the addition of adjuvants may render the compounds less toxic to man. Absorption is mainly through the skin or by inhalation and occasionally ingestion, and although the main action is the inhibition of cholinesterase, there is also inhibition of lipase, hepatic esterase, and beta-esterase. For treatment the author advises atropine, ganglioplegics, central stimulants, P2-AM (pyridine-2-aldoxime methoiodide) which reactivates the enzyme, but is not efficacious on all the phosphoric esters, *e.g.* OMPPA (schradan; octamethyl-pyrophosphoramide).

5 fatal cases in agricultural workers are then described, the oldest being 20 and the youngest 15 years of age. All were quite inexperienced and had been acting as assistants to the sprayer, making up the mixture and carrying it to him. 3 were found unconscious and all died within a few hours. In none of the cases had any precautions whatever been taken. As regards preventive measures, in addition to the necessity for proper protective clothing, eye shields, etc., the author considers that propaganda by every means available is required as to the dangers of these organic phosphorus compounds and the care required in their use, including instruction for operators, sprayers, etc.; improvement of first aid measures is urgently necessary to avoid loss of precious time in removal to a properly equipped hospital. The ENPI [National Bureau for the Prevention of Accidents] at Naples has already started an extensive campaign on these lines which has aroused considerable interest.

W. K. Dunscombe

DURHAM, W. F., HAYES, W. J., Jr. & MATTSON, A. M. **Toxicological Studies of O,O-Dimethyl-2,2-Dichlorovinyl Phosphate (DDVP) in Tobacco Warehouses.** *Arch. Indust. Health.* Chicago. 1959, Sept., v. 20, No. 3, 202–10, 2 figs. [11 refs.]

"Tests have been carried out in tobacco warehouses to determine the toxicity of DDVP (O,O-dimethyl-2,2-dichlorovinyl phosphate) to mammals and its effectiveness against the cigarette beetle. The insecticidal aspect of the work has been presented elsewhere. In some tests, DDVP was dissolved in perchlorethylene and sprinkled on the floors; in other tests it was applied as a thermal aerosol. Dosage levels studied were 0.5, 1, 2, and 10 mg. per cubic foot. Human volunteers spent up to eight hours per day and rats and monkeys were confined continuously in the treated warehouses. Concomitant studies of concentration of DDVP in the air were made. No signs or symptoms of DDVP intoxication were noted in volunteers or experimental animals. All species showed some degree of cholinesterase depletion after exposure to the highest DDVP application. Aerosol application of DDVP produced less cholinesterase effect than did sprinkling of a perchlorethylene solution of DDVP. It is concluded that DDVP would be safe for warehouse workers when applied twice a week or less often at a rate of 2 mg. or less per cubic foot as a thermal aerosol."

SAYNISCH, F. Hautschäden bei der Chloromycetinherstellung [**Dermatoses in Chloramphenicol Manufacture**] *Berufsdermatosen.* Aulendorf. 1959, Aug., v. 7, No. 4, 198–204, 3 figs.

Side effects in chloramphenicol therapy are rare but in the synthesis of this antibiotic, the chemical stages of which are described here at some length, there are intermediate substances which may cause skin disease in the exposed workers. The author of this paper describes his experience of 15 workers who after 8 to 15 days of contact with *p*-nitrobromacetophenone suffered from a dermatitis of the hands and forearms which in some instances extended to the face and neck. In these patients the dermatitis was of toxic nature and did not recur in the workers when conditions of production were improved in 1955. In 1958 a worker who had been employed in the factory for some years developed a skin condition which was particularly severe and he was admitted to hospital. The diagnosis made on the results of tests which are recorded was "an allergic contact" eczema due to *p*-nitrophenylaminopropane diolhydrochloride which is also an intermediate in the synthesis of chloramphenicol. It is stated that this particular allergic state, the manifestations of which recurred in this patient, has not been described previously. *M. E. Delafield*

HYATT, E. C., MOSS, W. D. & SCHULTE, H. F. **Particle Size Studies on Uranium Aerosols from Machining and Metallurgy Operations.** *Amer. Indust Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 99–107, 6 figs.

The mass median sizes of uranium oxide (U_3O_8) dusts were determined from measurements of alpha

activity on each of the 4 cascade impactor sampling plates by using a calibration carried out by visual counting in the laboratory and checked by chemical analysis. The oxide was produced during production processes on normal and enriched uranium metal, the latter having 100 to 200 times the activity of the former.

Extracting uranium castings from graphite moulds and cleaning up the moulds with vacuum cleaner and wire brush released particles with an average mass median diameter up to 3·6 microns. The exhaust dust from the hoods was about one micron finer than the general foundry airborne dust since large particles tended to escape the suction into the hoods.

Machining operations generate coarse dust from the first cuts into the oxidized surface of castings. During machining the chips may burn, owing to the heat generated by the cutting tool, and produce a very fine smoke. A coarser dust is released when the operator brushes away the swarf into the pan of coolant. These factors caused a wide range of sizes, from 0·4 to 3·9 microns, to be observed. Other operations yielded particles in the same size range.

Particle size was also determined for enriched uranium by counting the alpha tracks emanating from each active particle. A strip of photographic emulsion was laid over the sample, left for five days and developed "in situ". A particle of 1 micron then produced 2 tracks; up to 100 tracks per particle can be counted accurately. The method was unsuitable for normal uranium on account of its low activity which would necessitate exposure of 39 months.

C. N. Davies

KLEINFELD, M. & ABRAHAMS, A. P. **Administrative Experience with Occupational Overexposure to Radiation.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug., v. 20, No. 4, 294–8.

This paper contains an analysis of the 19 instances of excessive radiation exposure which have been reported to the New York State Labor Department and investigated by its Division of Industrial Hygiene since December 1955, when Industrial Code Rule 38 became effective. This Code defines overexposure as "a known or suspected dose of more than 3 rems of external radiation or an equivalent internal exposure from inhaled or ingested radio-active material over a 13 week period".

The results of the investigation are fully described with detailed tables. 8 of the reports of excessive radiation were found not to involve overexposure of personnel. The details of chronic or acute overexposure to external or internal radiation which are given include the source of overexposure, number of employees exposed, estimated dose, positive biological data, corrective measures instituted and the causal factors of overexposures. There were 11 instances of actual overexposure—4 chronic in nature, 4 acute external and 3 acute internal. 10 employees showed positive biological effects such as radiation burns, most frequently on the hands with or without abnormal retention of radioactive material. "In general the data indicates that the incidence of radiation overexposure (1·4 per cent.) and injury (0·3 per cent.) in New York State is extremely low when compared to other major industrial hazards".

M. E. Delafield

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

WELCH, H. **Problem of Antibiotics in Foods. [Report to the Council on Foods and Nutrition** (WHITE, P. L., Secretary).] *J. Amer. Med. Ass.* 1959, Aug. 22, v. 170, No. 17, 2093–6.

The author is Director of the Division of Antibiotics of the United States Food and Drug Administration. He estimates that between 17 and 20 million inhabitants of that country "may react to contact with antibiotics" and discusses whether this may be due to the presence of these drugs in food. The use of antibiotics as animal feed supplements and as crop sprays is innocuous, since no antibiotic should be in the final product. It has been permissible for some years under certain conditions to use tetracyclines as preservatives for poultry, and permission for this has recently been extended to fish, but not so far to meat: the small amounts of antibiotic permitted to remain in poultry and fish are said to be destroyed by cooking. Milk is a different matter, owing to the use of antibiotics for the treatment of mastitis, and in 1954–56 6·9% of 2,274 samples of milk from all States in the Union contained detectable penicillin. Since then it has been made illegal for a penicillin preparation for the treatment of mastitis to contain more than 100,000 units per dose, and a campaign has been undertaken to dissuade the farmer from marketing milk from a treated animal or area until 3 days have elapsed. In 1958–59 the percentage of 1,170 samples of milk containing penicillin fell to 3·7.

L. P. Garrod

FOOD POISONING

FABIANI, A. Osservazioni sopra un episodio di tossinfezione alimentare da stafilococco enterotossico alla luce dell'indiagine epidemiologica [**Staphylococcal Food Poisoning**] *Riv. Italiana d'Igiene.* 1959, Jan.–Apr., v. 19, Nos. 1/4, 87–96. English summary (5 lines).

Two outbreaks of staphylococcal food poisoning are described which occurred at Savona in 1957. In the first, 6 persons in a merchant ship in the port and 3 living in the town were affected with the usual symptoms 6 hours after a meal. All had bought cream cakes from a confectioner's shop which also made the cakes. A few days later another 10 persons were also affected and again they had eaten cakes from the same shop. In the first instance all examinations were negative and the shop was kept in excellent condition, but on the next occasion an enterotoxic staphylococcus was isolated not only from the cream cakes but also from the nose of a young female employee engaged in selling (but not making) the cakes.

7 months later another 7 persons were definitely and others probably affected with the usual symptoms and again they had eaten cakes from the same shop. An enterotoxic staphylococcus was isolated from the cream but all the staff were negative and the origin of the outbreak was not discovered. *W. K. Dunscombe*

ALI, S., RASOUL, K., MOHAMED, A., SAFI, G. & KRISHNAN, K. V. **An Outbreak of Encephalitis in a Village in Afganistan.** *Indian J. Pub. Health.* 1959, July, v. 3, No. 3, 279–82, 1 map.

An outbreak of encephalitis comprising 27 known cases with 14 deaths occurred in May–June 1958 in an Afghanistan village. 8 patients who had just passed the acute phase were observed in hospital. The village had 80–100 houses with about 1,000 inhabitants, the houses being in several clusters ½ to 1 kilometre apart.

A cow said to have been sick and unable to walk was slaughtered and eaten by one family and their friends. The family of 16 all developed the disease and only 2 survived. Two friends also were attacked, but recovered. One of the family who recovered was nursed in another house where one non-fatal case occurred. Another family of 4 who were friends were affected, but recovered—the disease, however, affected another family of 4, one of whom had nursed a case—all of these recovered. No further cases occurred.

Onset was sudden with severe headache, pain in the shoulders, nausea and constipation. None had fever. Giddiness, mental dullness, difficulty in walking and speaking, and prostration followed. These lasted 3 days and were followed by coma for about 4 days, after which the patient either died or recovered. Recovery was complete 3 weeks after onset. No marked changes in the reflexes were found. No post mortem examinations were made. Paired sera from 3 cases were examined for antibody against arthropod-borne encephalitis viruses with negative results. Only 1 patient had a leucocytosis and no changes were found in the cerebrospinal fluid.

Domestic animals in affected houses appeared to be involved. Another cow was seen which was unable to walk and had a large number of ticks attached. A dog was seen in coma. 20 chickens and 2 cats were also said to have died of the disease.

The authors consider that a neurotoxin in the food is the most probable explanation of the outbreak. *C. E. Gordon Smith*

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

GRIN, E. I. & OZEGOVIC, L. Problemi attuali delle dermatomicosi in Iugoslavia. [**Present Position Regarding Dermatomycoses in Yugoslavia**] Reprinted from *Minerva Med.* 1959, Apr. 25, v. 50, No. 33, 1245–51, 2 figs. [35 refs.]

Between 1954 and the middle of 1958 the Central Mycological Laboratory in Serajevo isolated a total of 13,775 strains representing 9 different dermomycotic species from cases of ringworm and favus: over 66% of these strains were *Tricophyton violaceum* and over 30% *T. schonleini.* Reasons are given in this paper against any aetiological connexion between endemic ringworm in the population of Yugoslavia and mycotic reservoirs in bovines or the soil.

Ringworm in Yugoslavia is a family disease, not limited to children; each case found among schoolchildren represents on an average 2·6 cases in the general population. As high a proportion as 90% of the inhabitants of some towns and villages have been examined with positive findings ranging between 23 and 72 per 1,000. The whole family must be examined and, where necessary, treated if the endemic is to be controlled. Ringworm does not spontaneously disappear at puberty, though clinical signs are more difficult to find in adults. Women are much more often

affected than men. The nails were involved in 3·2% of the cases. Trauma, acute infections and ill-health are believed to be contributory factors.

Since 1952 a mass diagnosis and treatment campaign has been carried out in Serbia, in Bosnia and Hertzegovina and, to a lesser extent, in Macedonia. By 1958 an aggregate of 1,335,420 inhabitants had been examined and 59,886 found affected with ringworm or favus. In some localities those over 18 years of age were excluded from the survey. Diagnosis was based on microscopic examination and, in many cases, the species was identified by culture. Treatment is by X-ray depilation made available at mobile or otherwise temporary centres when necessary. The aim is to eradicate the disease or to bring it down to such levels as can be controlled by the local public health services.

J. Cauchi

Anais Inst. Med. Trop. Lisbon. 1958, Dec., v. 15, No. 4, 867–77. Tinhas humanas em Cabo Verde. I. Estudo etiológico de alguns casos das ilhas da Boa Vista e de S. Nicolau [De Meira, M. T. V., Nogueira, J. P. & Simoes, T. S.], 867–9. [**Tinea in Man in Cape Verde. I. Aetiological Study of Cases in Boa Vista and S. Nicolau**] II. Estudo etiológico de alguns casos da ilha de Santo Antão [De Meira, M. T. V., Nogueira, J. F. P. & Coito, A. M.], 871–2. [**II. Aetiological Study of Cases in Santo Antao**] III. Agentes etiológicos de Tinea capitis na ilha de S. Vicente [De Meira, M. T. V. & De Sousa, H. T., with the technical collaboration of M. A. Coutinho], 873–7, 2 figs. on pl. [**III. Aetiological Agents of Tinea Capitis in S. Vincent**].

The English summaries appended to the paper are as follows:—

I. "During the time that a mission of studies was in Cape Verde, in 1946–47, the authors found some cases of *Tinea capitis* among the natives from the islands of Sal, Boavista and S. Nicolau, of which five cases were due to *T. ferrugineum* and ten to *M. felineum*."

II. "In 1948 the authors visited the island of Santo Antão (Cape Verde islands) having seen 17 cases of *Tinea capitis*, 9 of which were due to *M. felineum* and 1 to *T. ferrugineum*."

III. "The authors observed 165 cases of *Tinea capitis* in Saint Vincent (Cape Verde islands), being 163 positive by direct examination. The culture in 106 cases showed that 104 of them were due to *Microsporum felineum*, 1 to *Trichophyton acuminatum* and 1 to *Trichophyton rubrum*."

Fedors, P. **Inhibition of *Histoplasma capsulatum* and *Blastomyces dermatitidis* by *Pseudomonas aeruginosa in vitro*.** *Mycopathologia.* The Hague. 1959, Sept. 15, v. 11, Nos. 1/2, 128–34.

"It was accidentally discovered that *Pseudomonas aeruginosa* inhibited the growth of *Histoplasma capsulatum* when both of the organisms were isolated from a series of sputum specimens obtained from a single patient. Experiments were performed to determine if there is any inhibitory effect on other systemic fungi.

"Three fractions were obtained from a broth culture of *P. aeruginosa* and their antibiotic effects tested against various systemic fungi and bacteria."

Howard, D. H. **Observations on Tissue Cultures of Mouse Peritoneal Exudates inoculated with *Histoplasma capsulatum*.** *J. Bacteriology.* 1959, July, v. 78, No. 1, 69–78, 7 figs. [32 refs.]

This work was undertaken with a view to evaluating the usefulness of cell culture techniques in the examination of problems of the host-parasite relationship in human mycoses on a cellular level. Glycogen-induced peritoneal exudates consisting at first of a variety of cell types but later mainly of histiocytes (macrophages) were inoculated with a 3×10^5 yeast phase suspension of *Histoplasma capsulatum*. At 24 hours after inoculation many of these macrophages were engorged with *H. capsulatum* yeast phase cells. At 48 hours these cells were no longer visible, having been either digested by the macrophages or become tinctorially undetectable. Macrophages infected by *H. capsulatum* eventually degenerated, exhibiting cytoplasmic shrinkage and markedly pycnotic nuclei. Eventually they ruptured, thus liberating the yeast cells which were then free to infect other macrophages. Inoculation of macrophage cultures with the mycelial phase of *H. capsulatum* resulted in a rapid conversion of this phase to the yeast phase. In due course such tissue cultures were wholly destroyed by the activity of the parasite. It was therefore somewhat disconcerting to find that the non-pathogenic yeast *Saccharomyces cerevesiae* was able to destroy macrophages in these tissue cultures with almost equal facility.

C. J. La Touche

Van Laethem, R., Thys, A. & Vanbreuseghem, R. Troisième cas congolais d'histoplasmose par *Histoplasma duboisii* Vanbreuseghem 1952. [**Third Case of *Histoplasma duboisii* Infection in the Belgian Congo**] *Ann. Soc. Belge de Méd. Trop.* 1959, June 30, v. 39, No. 3, 319–29, 4 figs. on 2 pls. [11 refs.]

The English summary appended to the paper is as follows:—

"The authors report the third Congolese case (26th in the world literature) of histoplasmosis due to *H. duboisii* in an African child $2\frac{1}{2}$ years of age. The skin, glands, bones and viscera were invaded but not the lungs, and the condition ended fatally. The fungus responsible for the condition was isolated and successfully inoculated into guinea-pigs and hamsters. Search for persons positive to histoplasmin has shown that histoplasmosis is widespread in the region."

Heyn, Ruth M. & Giammona, S. T. **Disseminated Histoplasmosis treated with Amphotericin B.** *J. Dis. Children.* Chicago. 1959, Aug., v. 98, No. 2, 253–6. [21 refs.]

An infant of 5 months suffering from disseminated histoplasmosis as shown by positive marrow and spleen cultures, was treated with Amphotericin B given by

intravenous drip for 21 days to a total dose of 120 mgm. He became afebrile after 4 days' treatment; on the 10th day he began to gain weight and he was discharged well 28 days later. At the age of 18 months he remained normal.

This is the first recorded case of an infant being successfully treated with Amphotericin B. The recommended initial daily dose is 0·5 mgm./kgm. of body weight increasing to 1·0 or 1·5 mgm./kgm. per day in the absence of toxic effects. *Peter Abbott*

PROSPERO, Magdalena T. & REYES, A. C. **The Efficacy of Corn Meal Agar, Soil Extract Agar and Purified Polysaccharide Medium in the Morphological Identification of** *Candida albicans*. *Acta Med. Philippina*. 1955, Oct.–Dec., v. 12, No. 2, 69–74.

The increasing recognition of the yeast-like organism *Candida albicans* as a pathogen, especially in its secondary role complicating pre-existing disease during antibiotic therapy, necessitates a corresponding effort to develop more critical methods of identification. The authors of this article record the results of their comparative study of the culture of this organism simultaneously on 3 impoverished media which have been widely used for identifying this species, namely, corn meal agar, soil extract agar and purified polysaccharide medium; chlamydospore production being the accepted morphological criterion of identification for *C. albicans* on such media.

290 yeast colonies isolated in culture on Sabouraud's agar from the mouths of babies were tested simultaneously on these 3 culture media. Results show that corn meal agar stimulated the production of chlamydospores in 149 colonies (51·0%); soil extract in 103 (35·0%) and purified polysaccharide medium in 94 (32·0%). However, in spite of the manifestly superior efficacy of corn meal in providing the greatest number of positive identifications, it was found that an additional 9·7% of the total number of colonies tested were stimulated to produce chlamydospores by the soil extract agar or by the polysaccharide medium, or both, when corn meal agar had failed to do so. Accordingly, the authors advocate the simultaneous use of these 3 diagnostic culture media for optimum results in the identification of *C. albicans*. *C. J. La Touche*

MONASH, S. & ROTH, F. J., Jr. **The Effect of X-Rays, Grenz Rays, Thorium-X, and Radioactive Phosphorus on Superficial Mycotic Agents.** *Arch. Dermat.* 1959, Sept., v. 80, No. 3, 288–93, 4 figs.

"All forms of ionizing radiation tested, namely α-rays of thorium X, β-rays of P^{32}, as well as x-rays of different wave lengths, produced inhibition in growth of several pathogenic fungi. In some strains subinhibitory doses appeared to produce a stimulatory effect as shown by an acceleration of growth and the production of an increased number of conidial structures. Colonies exposed to a near-lethal dose were generally characterized by a loss or reduction in the numbers of defined morphologic entities. In some cases variations in pigment production and mycelium formation were observed.

"Complete inhibition of fungi with x-ray required from 200,000 to 300,000 r units and with Grenz rays, 390,000 to 600,000 r units. With C. albicans, 190,000 r units of Grenz rays produced complete inhibition."

HOWELL, A., Jr., MURPHY, W. C., PAUL, Frances & STEPHAN, R. M. **Oral Strains of** *Actinomyces*. *J. Bacteriology*. 1959, July, v. 78, No. 1, 82–95, 15 figs. [Numerous refs.]

In order to test previous claims that species of *Actinomyces* identical or nearly so with species isolated from lesions could be obtained from normal mouths the authors undertook a critical study of some 200 strains isolated from normal human mouths, and, for comparison, 11 strains isolated from human lesions. Two major types of oral actinomyces were isolated on the basis of type of growth of initial cultures in fluid thioglycolate medium and morphology of micro- and mature colonies on brain infusion agar. Type 1 comprised 42 of the strains considered in this study. Of these, 31 strains were isolated on blood plates which were incubated aerobically, but it seems that, in the case of these strains, ability to produce aerobic growth depended both on the amount of inoculum seeded and the culture medium selected. They differed from species of *Nocardia* in so far as they were catalase-negative and facultative or microaerophilic. The authors are of the opinion that they were similar to those described by THOMSON and LOVESTEDT [this *Bulletin*, 1951, v. 26, 1129] as *Actinomyces naeslundi* and should be considered as such.

The strains of this species are said to differ from those of *A. israeli* in the following characters: ability to grow more frequently from plates incubated aerobically rather than anaerobically; usually rapid diffuse or flaky growth in thioglycolate medium; reduced amount of mycelium of briar type with uneven branching on brain infusion agar and, on this medium also, mature colonies within a given strain may be rough or smooth or both; raffinose is usually fermented but not mannitol or xylose; nitrate is reduced to nitrite by nearly all strains; many strains are able to grow in media containing 10–20% bile, and, finally, tolerance to oxygen is exhibited by most strains of this species. On the whole, the strains designated by the authors as Type 1 *Actinomyces* exhibited a similar behaviour.

Type 2 organisms were isolated anaerobically on blood agar with 5% CO_2 and 95% N_2. On thioglycolate medium growth was slow and in the form of "discrete, variably sized, lobulated granules, with about one-third growing as tiny discrete granules". On brain heart infusion agar "the filaments were slender, of variable length, straight or slightly tortuous, nonseptate, and freely branched with the branches arising singly, and at an acute angle". Mature colonies on this medium exhibited much variation in their gross characters, thus: round entire, strongly convex to pulvinate with a finely granular or pitted surface; or heaped rounded and finely lobate; or heaped cerebriform to coarsely lobate with an irregular, lobate edge; or very heaped, bread-crumb or cauliflower-like; or,

finally, irregular very heaped, raspberry-like with or without a central crater. Their colour was creamy white but occasionally greyish white. Growth and fermentation reactions exhibited by strains of this type in sugar solutions were so variable that it was possible to subdivide them into 3 groups on the basis of these reactions, but in the authors' opinion this did not seem to be warranted in view of their close resemblance in other major characteristics. Furthermore, Type 2 strains "were identical in nearly all major respects with 10 strains of *A. israelii* isolated from human lesions".

C. J. La Touche

HEINRICH, S. & PULVERER, G. Zur Ätiologie und Mikrobiologie der Aktinomykose. III. Die pathogene Bedeutung des *Actinobacillus actinomycetemcomitans* unter den "Begleitbakterien" des *Actinomyces israeli*. [**The Aetiology and Microbiology of Actinomycosis. III. The Pathogenic Significance of *Actinobacillus actinomycetemcomitans* among the Bacteria isolated together with *Actinomyces israeli***] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 176, Nos. 1/2, 91–101. [20 refs.]

The English summary appended to the paper is as follows:—

"Former investigations (I. Communication of this series) revealed that the special significance of mixed infections of human actinomycosis seems to lie in the metabolic cooperation with actinomyces israeli. Without this cooperation the disease evidently does not start.

"Among the bacteria accompanying actinomyces actinobacillus actinomycetem-comitans seems to play a special part in the pathogenesis of actinomycosis. Up to the present this cooperation was only assumed but never proven.

"This paper presents significant, certified facts proving the facultative pathogenetic qualities of this microorganism, which plays a leading role among the mixed bacterial flora of actinomycosis. Again it also could be confirmed that actinobacillus actinomycetem-comitans is part of the normal oral flora."

[See this *Bulletin*, 1959, v. 34, 442.]

LIE-KIAN-JOE, NJO-INJO TJOEI ENG, TJOKRONEGORO, S., SCHAAFMA, S. & EMMONS, C. W. **Phycomycosis of the Central Nervous System, associated with Diabetes Mellitus in Indonesia.** *Amer. J. Clin. Path.* 1959, July, v. 32, No. 1, 62–70, 5 figs. [17 refs.]

15-year-old diabetic girl was admitted to hospital in Djakarta with a tumour-like mass involving the left nasal cavity and left orbit. There were signs of cranial nerve involvement and a tentative diagnosis of nasopharyngeal tumour with extension into the cranial cavity was made. At autopsy a friable mass continuous with that in the nasal cavity was found attached to the dura and there was extension into the brain substance. In addition there was a separate abscess cavity in the left frontal lobe and complete thrombosis of the left internal carotid artery.

Sections from the affected tissues showed the presence or irregular, septate branching hyphae surrounded by a necrotic reaction and granulomatous formation. Unfortunately, all cultures were heavily contaminated and a causal fungus could not be isolated.

The lesions were considered to be due to invasion by a member of the Phycomycetes and the term phycomycosis is suggested as appropriate for such invasion where the specific organism cannot be identified. 5 cases of this condition have been observed in Indonesia since 1956 and this is the fourth to be reported [see, for example, this *Bulletin*, 1957, v. 32, 327].

Peter Abbott

See also p. 18, BRINGHURST, BYRNE & GERSHON-COHEN, **Respiratory Diseases of Mushroom Workers. Farmer's Lung.**

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

HEAF, F. **The New Epidemiology of Tuberculosis.** *Med. Officer.* 1959, Aug. 21, v. 102, No. 8, 71–5. [21 refs.]

After pointing out the importance of the changes in epidemiology in countries with well developed health services, Heaf suggests that the pattern of disease in many of the overseas countries is similar to that which existed in great Britain 50 years ago. He then discusses the main changes in Great Britain. Comparing figures here and in New York it is interesting that in 1957 the percentage of advanced cases among those

picked up by mass radiography was 13·4% in Edinburgh, and 28% in New York.

The first half of the paper is summarized under 10 headings given below.

"(1) The mortality and morbidity from respiratory tuberculosis is highest in the elderly age-groups in males and the early middle-age groups in females.

"(2) The positive tuberculin reaction, which may be considered as synonymous with infection, is becoming progressively less frequent in children but is common in adolescence and is usually present by the age of 35 years.

"(3) The negative tuberculin reaction is not infrequently found in elderly males in certain areas. The exact significance of this is not yet known.

"(4) Infection by drinking tuberculous milk is now very infrequent in most areas in Great Britain. Infection is now mainly from man to man and the possibility of man infecting cattle will have to be considered in the future.

"(5) Infection by drug-resistant organisms is increasing, thereby creating a type of lesion about which little is known and which is difficult to treat.

"(6) The virulence of INAH drug-resistant strains that are catalase negative is considerably decreased.

"(7) INAH appears to confer some degree of protection against virulent infection in guinea pigs.

"(8) INAH-resistant BCG strains possess immunizing powers of the same order as INAH-sensitive BCG.

"(9) The disease is frequently symptomless, even in its advanced stages.

"(10) There is a seasonal variation in both mortality and morbidity curves."

He then moves on to the modification in preventative methods which this involves. These of course are more controversial. It is suggested that in communities where the percentage of tuberculin reactions is above 20% in the 12–13 age-group vaccination of the lower age-groups is advisable. Where the percentage of reactions in the 5-year age-group is above 20, newborn babies should be vaccinated. If the percentage in the 12–13 age-group falls below 10 vaccination except of contacts is debatable as the value of the tuberculin test is lost.

Primary infection should be discovered as early as possible after infection. The child must be examined for active tuberculosis, especially if the patient has a high grade reaction, and the source of infection should be searched for diligently. All reactor children under 3 years of age and all with any evidence of activity must be treated with orthodox drugs. If doubtful a course of isoniazid should be given. Patients harbouring resistant organisms should be treated in hospital.

A table is given embodying the above suggestions and many others.

[This brilliant paper must be read by all those who deal with tuberculosis, especially from the public health aspects. The journal in which it appears is often not on the list of those read regularly by chest clinic physicians. The Ministry of Health would do well to distribute reprints to all clinic physicians and health visitors.] *F. H. Young*

ANDERSON, J. P. **Deaths from Pulmonary Tuberculosis in Leicester during 1956 and 1957.** *Tubercle.* 1959, Apr., v. 40, No. 2, 99–105. [11 refs.]

Where diagnosis and treatment are adequate, deaths from pulmonary tuberculosis should only occur in exceptional circumstances. Accepting this the author of this paper tries to find out why 56 patients were registered as dying from this disease in 1956 and 1957 in the City of Leicester. 15 were considered to have died from some other cause, leaving 41; 9 men and 8 women were between 25 and 45 years of age, but 18 men and 6 women were over 45. The author presumably felt that in many instances several factors were responsible for the deaths as he does not include a tabulated report.

Of the 22 patients who died in 1957, 4 failed to consult their doctor. 2 women died after pregnancy, no X-ray having been taken; in 3 patients the family doctor was slow to come to a diagnosis, and in 3 there was a failure to diagnose and treat active disease in patients who had been considered quiescent. In 10 patients associated disease was a factor in death; 9 of them had chronic bronchitis and 4 were psychiatric casualties.

Drug resistance as a result of treatment was much commoner in 1957 than 1958. 16 patients failed to cooperate in treatment and this was a factor in their early death. 3 patients died after operation. The author discusses how the mortality can be reduced, but human error and resistance by patients will prevent 100% success.

[See also this *Bulletin*, 1957, v. 32, 841.]

F. H. Young

EMERSON, P. A. **Tuberculosis Contacts in North-West London.** *Tubercle.* 1959, June, v. 40, No. 3, 177–80. [12 refs.]

This paper contains an unusual approach to the estimation of the likelihood of the development of tuberculosis in contacts. It reports the likelihood of its development in contacts who were healthy at the time when the original patients became apparently non-infective. 1,517 household contacts of patients who had become non-infectious or were no longer in contact with the patients are dealt with. 85 (5·6%) of the contacts were found to have tuberculosis on the initial examination and are removed from the study, leaving 1,432; of these, 57 (3·8%) developed tuberculosis within 5 years. A complete 5-year follow up was impossible, but reasons are given for thinking that this lack had little effect on the results. Of the 57, 6·6% occurred in the 6–15 age group: it is interesting that this age group produced nearly the lowest percentage of cases at the original examination. The proportion of initial and subsequent cases was higher in siblings than in the other relations of contacts.

The date of development of tuberculosis year by year in the various age groups is given; as might be expected the greatest incidence was found to be in the first year, and tuberculosis developed sooner after the initial examination in the younger age groups.

The important conclusion that emerged from the study was the high incidence of tuberculosis which

appeared in the 6–15 age group. There has been a tendency recently to assume that after a single X-ray examination this age group can be left to itself until puberty; but if the conclusions of this paper are accepted, regular annual radiology is the minimum that should be carried out. *F. H. Young*

FLETCHER, W. B., MAIR, J. M., SKLAROFF, S. A. & WILLIAMSON, J. **Observations on Non-Attendance in a Community Chest X-Ray Survey.** *Tubercle.* 1959, Apr., v. 40, No. 2, 82–92, 2 figs.

The Edinburgh X-ray campaign of March 1958 [this *Bulletin*, 1959, v. 34, 427] succeeded in examining 76·6% of the population over 15 years of age (360,924), and this was raised to 84·4% when patients X-rayed in connexion with the campaign, but not actually examined during the 25 days of it, were included. An endeavour was later made to examine the remainder, and to find out why they had failed to be X-rayed. This was confined to all persons in a typical city ward with a population of 13,012 at risk—a full supplementary survey was impracticable.

Repeated visits were made by health visitors and doctors to all people who had been missing, and a full account of the methods used is given. It is difficult to see how more could have been done. 10% of the people on the original list were found to have gone away or died. 233 persons had had unverified X-ray examinations, leaving 1,570 who had definitely failed to be X-rayed Of these, 262 were never available owing to absence during the whole period, leaving 1,308 to be recanvassed. Of these, 526 were X-rayed as a result of the canvass. Full details are tabulated.

The reasons for failure were diverse; some people were non-cooperative, some claimed that they had been recently X-rayed, but in many cases this could not be verified; some were immobile. A full classification is given.

The percentage of tuberculosis was significantly greater for males of all ages in the supplementary survey, but the numbers were insufficient to allow significant figures in the various groups, except for active tuberculosis in males between 35 and 64 years. In females only tuberculosis of doubtful activity in those aged 65 or more was significantly higher in the supplementary survey. For the future all notified cases are to be checked against these classifications in the main and supplementary surveys. It would appear that 90% of people on an electoral roll is the highest proportion who can be X-rayed voluntarily.

This is a very illuminating paper. *F. H. Young*

L'ELTORE, G. Attualità in campo tubercolare. [**The Present-day Position in Tuberculosis**] *Lotta c. la Tubercolosi.* 1959, May, v. 29, No. 5, 561–88. [Refs. in footnotes.] English summary.

After reviewing briefly the principal causes of death in Italy at present where tuberculosis (all kinds) occupies 9th place, the author shows that in the last 70 years the mortality for this disease has fallen less than for other infectious diseases though since 1946 there has been a considerable fall.

Figures are given, obtained from a pilot survey conducted by the Central Statistical Institute in 1956, which covered 58,602 persons, 38,053 males and 20,549 females. Pulmonary tuberculosis formed 87% of the total.

Females were more affected than males in all forms of primary tuberculosis and in the post-primary forms of the exudative kind including pleurisy; males were more affected in the fibrocaseous and cavitating forms. About 25% were between 25 and 35 years, and 14·5% were over 55 years old; males predominated here, thus confirming the opinion that the pulmonary disease is tending to become largely a disease of older men. In 53% of the pulmonary cases there was an interval of more than 6 months between diagnosis and sanatorium treatment, males being admitted notably later than females. More than 75% had only medico-sanatorium treatment, 4·5% surgical, and 20% collapse (pneumothorax) and while the last is tending to decrease, surgery is increasing particularly for segmental resection.

The author is not generally in favour of surgery for the pulmonary form as he points out that a post-operative sanatorium environment may favour reactivation of the lesion, and since too early discharge is not the answer, he suggests that such patients should be isolated in the sanatorium away from sputum positive cases, and emphasizes less post-sanatorium and better sanatorium assistance.

Passing to diseases of the lungs generally the author states that a survey conducted by the Central Statistical Institute in 1955 on patients admitted to hospital gave 250,000 for chest conditions out of a total of 2½ million admissions. 8,794 had lung cancers, the proportion of males to females being 4 : 1. *W. K. Dunscombe*

MERENDA, P. & FORTUNI, M. La malattia tubercolare nel personale dell'Ospedale sanatoriale "P. Grocco" dal 1935 al 1957. Nota clinico-statistica. [**Tuberculosis in the Staff of the Sanatorium "P. Grocco" from 1935 to 1957**] *Lotta c. la Tubercolosi.* 1959, June, v. 29, No. 6, 756–72, 8 figs. [31 refs.]

This sanatorium was opened in 1935 and the investigation concerns staff taken on up to the end of 1957—a total of 385 persons. 32 who were on'y at work for less than 60 days have been lost sight of and are therefore outside the scope of this investigation. The paper deals with 353 persons, of whom 40 developed tuberculosis (11·33%), relapses not being counted in this figure. 25 cases (62·5%) were pulmonary, 11 (27·5%) pleural and 4 did not involve the respiratory system. 9 of the 25 pulmonary cases were exudative and 16 were proliferative in type. The numbers in this series are relatively small; the value of this study is in the care taken when such personnel is being selected for employment, the regularity of its duties, its planned feeding, its health control by periodic medical examination and the comparability of the hazards to which such individuals are exposed.

On the basis of the average size of establishment employed each year the tuberculosis morbidity rate was 17·73 per mille, but when the records are analysed in

5-year periods it is seen that the morbidity has been dropping in recent years; a 1942–45 peak is undoubtedly accounted for by the War. Those employed in the wards, laundry and disinfector and on the other more hazardous duties had higher morbidity rates and so had those within the first 2 years of service and the age group of 21–30 years. Allergy to infection is liable to rise in the first 2 years of employment and the authors advise prophylactic isoniazid during this initial period. Newcomers should at first be posted to those duties which entail less risk. No one under 25 years of age should be employed.

The findings of other research workers accord with the results of the investigation which is reported here.

J. Cauchi

INDIAN J. INDUST. MED. 1959, Mar., v. 4, No. 3, 1–41, 3 charts on pl. [11 refs.] **Tuberculosis in Industry.**

In the first paper (*Tuberculosis in Industry*, P. K. GHOSH, pp. 4–9) the author quotes BOGEN to the effect that there is in India a tuberculosis morbidity rate of 5 new cases per 1,000 of the population per annum. In Calcutta the death rate at age 21–30 in females was in 1952–3 3 times as high as in males and remained higher at all ages up to 50; this is very different from the situation in the West.

M. N. GUPTA (*Dust Inhalation and Pulmonary Tuberculosis in Industry*, pp. 10–17) reports studies on 1,612 workers in dusty industries with silica risk; 22% had silicosis and 9·4% tuberculosis. The incidence of tuberculosis was especially heavy (25·5%) in subjects with silicosis, and, in the pottery and ceramics industries, varied with length and intensity of exposure to dust.

N. PURSHOTTAM (*Tuberculosis in Industry in Bombay City*, pp. 18–23) writes in general terms on methods of detection in industry.

N. M. PANT, B. BANERJI and K. S. BASU (*Mass-Miniature Radiography in Industry*, pp. 24–29) report that in 3,069 employees of a large commercial firm in Bombay 6 per 1,000 were found by clinical examination to have tuberculosis, but in 2,373 of these submitted to miniature radiography the rate was 18 per 1,000; clinical examination is therefore not enough.

K. V. RAO (*Rehabilitation of the Tuberculous*, pp. 30–36) writes in general terms, and B. BANERJI, N. M. PANT and K. S. BASU (*Rehabilitation of the Tuberculous in Industry*, pp. 37–41) report on the 232 subjects with tuberculosis observed in one factory during the last 7 years, of whom 180 were rehabilitated within the factory. The average period of disability was 21 weeks and the average period on light work was 27 weeks. No details are given of the treatment adopted but modern drugs were evidently used.

[More information throughout this symposium on the type and severity of the disease and on the treatment and rehabilitation methods adopted would have added to its interest.] *Charles Wilcocks*

T'AO, J. C. **Tuberculosis in Taiwan (Formosa).** *Amer. Rev. Respiratory Dis.* 1959, Sept., v. 80, No. 3, 359–70, 8 figs. [12 refs.]

DEUSCHLE, K. **Tuberculosis among the Navajo. Research in Cross-Cultural Technologic Development in Health.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 200–206.

The Navajos, numbering about 85,000, are the largest Indian tribe in the United States. In 1955 a field health research project was started and this paper reports the results of investigations on tuberculosis. The Navajos believe that it is caused by improperly performed wind chants or contact with an object such as a tree struck by lightning. Although they and their medicine men agree in accepting modern treatment, they still hold their theory of causation; revealing anecdotes are related about these beliefs.

In 1950 tuberculosis was rife and miliary and meningeal tuberculosis were common. Between 2 and 3% had active disease and 50–60% of children aged 6–10 years were infected. An intensive programme of investigation and treatment was started in 1952, and in 1957 only 15 patients died of tuberculosis. In 1957 research covering an area containing 923 people was started. 81 had tuberculosis: of these 43 had arrested reinfection, 20 active reinfection, 13 active primary tuberculosis, and 5 chronic disease probably tuberculosis. The bulk of the cases throughout the tribe were obtained by following up tuberculin-positive children. The morbidity rate was 135 per 1,000 [? in] camps with tuberculin-positive children, and only 27 per 1,000 in camps with tuberculin-negative children. As a result of the hospitalization of infective patients, only 1 child has been observed to convert to positive. The Navajo Indians will readily accept treatment and react to it in the same way as other communities. Details are given of the methods employed. *F. H. Young*

ANDREWS, R. H. & RADHAKRISHNA, S. **A Comparison of Two Methods of Sputum Collection in the Diagnosis of Pulmonary Tuberculosis.** *Tubercle.* 1959, June, v. 40, No. 3, 155–62.

The 2 methods compared in this study were the examination of a single specimen ("spot" specimen) collected from the patient while attending the hospital for a medical examination and a pooled specimen of the sputum expectorated during the night away from the hospital. The specimens were examined by direct microscopy and by culture.

2 sets of each type of specimen were collected from each of 348 patients with bacteriologically proven tuberculosis and the results were:—

Specimens	Positive by Smear	Positive by Culture
1 "Spot"	66·1%	90·5%
2 "Spots"	76·4%	94·0%
1 "Overnight"	76·7%	93·1%
2 "Overnights"	83·0%	97·4%
All specimens	85·3%	99·4%

Most of these specimens were from patients with extensive disease, and the results show that a single specimen is of definite value, especially when the delivery of the overnight specimen to the hospital may be difficult as with patients in Africa. Further analysis of the results show, however, that when the specimens

are from patients with non-cavitated disease or from those undergoing effective chemotherapy the results of examining a single spot specimen are definitely less valuable than examining an overnight specimen.

S. R. M. Bushby

PARLETT, R. C. & YOUMANS, G. P. **An Evaluation of the Specificity and Sensitivity of a Gel Double-Diffusion Test for Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 153–66.

The tube method used in this extensive investigation was that described earlier [see this *Bulletin*, 1958, v. 33, 882] with the antigens present in 8-week-old cultures of H37Ra. The readings, which were recorded every day for 7 days, were based on the number of precipitating lines, 4-plus reaction for those with 4 or more lines, and 3-plus, 2-plus and 1-plus for those with the corresponding numbers of lines. To facilitate the analysis of the results, the patients were divided into 10 groups ranging from patients with well established non-tuberculous disease to those with very definite tuberculosis. Results were as follows:

	Diffusion Test Positive	
	Total	%
Non-Tuberculous (tuberculin positive 152)	466	2·1
Possibly tuberculous	89	27·0
Tuberculous		
advanced	380	84·2
moderately advanced	245	73·5
minimal	128	57·8
inactive	78	56·4
Extrapulmonary	41	43·9
primary	9	100·0
unclassified	76	68·4
patients with atypical acid-fast bacilli	140	74·3

From 83 patients more than 1 sample of serum was examined; in 36 the amount of antibody increased, 26 being negative and changing to positive, 30 showing no change and in 17 there was a decrease, 6 changing from positive to negative.

Sera from 11 medical students vaccinated with BCG were also examined; all developed antibodies in 8–12 weeks, but these did not persist in any for 20 weeks after vaccination.

These results are discussed at some length and the authors conclude that although the study did not meet all the requirements for an adequate assessment, the results indicate that the test holds considerable promise.

S. R. M. Bushby

SPIVEY, C. G. & WIER, J. A. **Tuberculous Polyserositis.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 259–61.

After pointing out that they are including patients who have only bilateral pleural effusion which some workers would not include under the term polyserositis, the authors discuss 22 cases of polyserositis seen at the Fitzsimons Army Hospital, Denver, Colorado, during a period of 4 years. The areas involved were bilateral pleural (11), pericardial and pleural (7), and peritoneal and pleural (4). Of the 11 patients with bilateral pleural effusions, 5 had no other demonstrable disease, 3 disseminated disease: 1 had miliary lung disease, 1 meningitis, and 1 renal and hepatic tuberculosis, and 2 had lymph node involvement. The main symptoms were toxic with pain in the areas involved. In 13 cases tubercle bacilli were recovered by one means or another. The age of the patients varied from 20 to 58, with only 2 over 31 years of age.

All patients recovered under antimicrobial drugs though some were inadequately treated by modern standards. 1 patient has had a serious relapse. In all cases where fluid was obtained it was exudate. Although allergy plays a part it is usually associated with a definite tuberculous infection of the serous membranes.

Although haematogenous spread may occur in some cases, the authors think that the main method of spread is by the lymphatics.

F. H. Young

MYERS, J. A. **The Natural History of Tuberculosis in the Human Body. II. Longitudinal Observations Imperative.** [Editorial.] *Amer. Rev. Respiratory Dis.* 1959, July, v. 80, No. 1, Pt. 1, 100–107. [Refs. in footnotes.]

This article is a comment on the long-term follow-up of patients diagnosed as tuberculous, carried out by Myers and his colleagues in Minneapolis, U.S.A., and made possible by the H. Longstreet Taylor Research Fund.

Reference is made to other long-term investigations by Paul D. WHITE (*Dis. of Chest*, Chicago, 1957, v. 32, 368) on pulmonary embolism, by T. GIESTLAND (*Acta dermat-venereol*, 1955, v. 35, *Supp.* 34, 1) on untreated syphilis, and by Sir R. PHILIP (*Trans. Tuberculosis Society of Scotland*, 1921–22, p. 4) on pulmonary tuberculosis. The present work was concerned with the fates of 160,000 university students, 6,000 private patients and 19,000 children observed from 1920–1; interim reports were published in 1954 and 1955.

The methods and difficulties met with are discussed. These are important as they stress the loss of material produced by lack of full records made at the time, destruction of case notes, and X-rays of patients who have been discharged as "cured". Brief though very interesting conclusions are given; for instance the X-rays of children who had negative tuberculin tests never revealed evidence of chronic pulmonary tuberculous lesions; even with positive reactions chronic clinical lesions were so rare that periodical X-rays are unnecessary until the age of 12–15 years. Primary pulmonary infiltrates were benign, the serious lesions in adolescents were confined to positive reactors so that the differentiation between primary lesions and endogenous reinfection lesions is essential in considering the results of treatment. As rigid contagious disease technique was instituted the infection of student nurses dropped; over half the student nurses were still uninfected on graduation. Among medical students 7·1% developed demonstrable tuberculous lesions before or after graduation; but among 1,218 uninfected on graduation 491 had become positive reactors, but only 0·66% had developed clinical lesions.

In 1,209 Law School graduates 1·33% had developed clinical lesions compared with the 7·1% among doctors.

The work is continuing. It explains Myers's opposition to the general use of BCG because of the loss of the essential tuberculin tests. *F. H. Young*

CROKAERT, J. Note sur les possibilités de guérison de la tuberculose ganglio-pulmonaire au Ruanda. [**Observations on the Possibilities of Spontaneous Cure of Hilar Gland Tuberculosis in Ruanda-Urundi**] *Ann. Soc. Belge de Méd. Trop.* 1959, Feb. 28, v. 39, No. 1, 25–40, 1 fig. [22 refs.]

In 1951 it was noted that in Ruanda-Urundi the highest morbidity from tuberculosis occurred in children from 6 to 10 years of age—3·49% in males and 2·94% in females. This compares with 1·06% in children between 4 and 9 years in Belgium in 1946. In the latter 96% healed spontaneously. It was decided to try to determine whether this occurred in the Belgian Congo. The histories of 117 children aged 2–17 years were followed for up to 3 years. After deducting those who died and for whom treatment was necessary, it was found that 78–83% could be expected to heal spontaneously. Considering the unfavourable circumstances which are detailed and compared with the conditions in Belgium, it is felt that this is satisfactory, but it is unfortunate that the proportion of children aged 6–10 years is not given. Detailed reports of a number of cases are given. *F. H. Young*

LUCCHESI, M., ZUBIANI, M. & CATACCHIO, L. Recidive dopo trattamento chemio-antibiotico e pneumotorace intrapleurico. [**Relapse of Tuberculosis after Drug and Collapse Treatment**] *Lotta c. la Tubercolosi.* 1959, May, v. 29, No. 5, 589–618. [49 refs.]

This paper is an extremely detailed account of the origins, bacteriology and treatment of relapse after treatment with drugs and intrapleural pneumothorax.

The authors define relapse as a new morbid tuberculous manifestation arising in a patient who has previously passed through a specific episode from which he was definitely clinically cured, and arising some months after clinical cure. They state that only by such a definition is it possible to be certain that it is not a renewal of a process not yet clinically cured and that numerous skiagrams and bacteriological and clinical tests are required before bases relating to cure and relapse are obtained.

Pathogenesis—tuberculous remnants such as fibrous scars which may occasionally reactivate, miliary foci or nodules, tuberculomas, filled-up cavities, and hilar-glands, are blamed for relapses; *initial disease*—this was mainly the diffuse exudative form particularly if bilateral, but the cavitating form was by far the most frequent relapse form even if the original lesion was not. An exogenous cause is very much rarer than endogenous as regards pathogenesis.

892 patients discharged clinically cured from the Carlo Forlanini Institute between January 1948 and April 1956 out of a total of 7,980 discharged in the same period are then discussed. 647 of them replied to a questionnaire and where possible were asked to return for re-examination [the figures for those who did are not given]. All had been treated by drugs with or without collapse therapy. They were subdivided as follows:—A, 433 given drug treatment only; B, 214 with collapse therapy as well; C, 388 treated in sanatorium; D, 259 part sanatorium and part ambulatory. Relapses occurred in 12·1%, most in Class B; Class C showed 9·7% against Class D 16·4%.

A more detailed investigation of 341 patients discharged between July 1954 and April 1956 gave total relapses as 8·5% (7·8% class A; 9·6% class B). Males relapsed more frequently than females. 12% were aged 26–30 years and 14·2% were over 40. Special emphasis is laid on the latter figure associated with the prevalence of the disease in older persons, particularly men.

The causes are mainly inadequate or incorrect drug treatment; the greater the dosage the less the chance of relapse, especially when 2 or more drugs are given together, and relapses are very much fewer with continuous than with intermittent treatment. Out of 98 cases 82·6% were sputum positive and though in 57 patients nearly half had streptomycin-resistant, 1/5th INH-resistant, and 1/7 PAS-resistant organisms, the results of biochemical tests, etc., showed that the bacteriological make-up of the organism had not changed. Relapses nearly always occur at the original site. For treatment, cycloserine, especially if combined with PAS intravenously, is very useful. The waiting period before collapse therapy must be very much shorter than in the original disease. Out of 647 of their patients discharged clinically cured 70 relapsed and in 146 relapsed patients 68·5% relapsed within 2 years after discharge. To avoid relapse the authors advise cycles of treatment, principally INH for at least 2 years after clinical cure [though even then 25 out of 146 relapsed]. The prognosis in relapse must be more guarded than for the original disease.

A much longer period than 2 years is necessary before the true percentage can be obtained as they found that out of the 146 relapse cases cited 25 occurred more than 3 years after discharge.

The authors conclude that relapses are most often due to unsatisfactory treatment in the broad sense of the word and that it is to a reduction in the number of relapsed cases that we should look for a reduction in mortality and general morbidity. *W. K. Dunscombe*

DRAIN, D. J., LAZARE, R. & TATTERSALL, K. **4-Aminosalicylic Acid Blood Levels following Oral Administration of Sodium 4-Aminosalicylate and Calcium 4-Benzamidosalicylate.** *Tubercle.* 1959, June, v. 40, No. 3, 201–4. [13 refs.]

The exact value of various preparations of PAS in preventing resistance to streptomycin and isoniazid is of great importance. After referring to recent publications on the subject, especially CaBPAS [this *Bulletin*, 1955, v. 30, 673; 1957, v. 32, 1143], the authors report a preliminary investigation on the blood levels produced by continuous administration of the drugs.

4 volunteers were given 4 gm. sodium PAS $2H_2O$ thrice daily and 4 others 4·7 gm. CaBPAS thrice daily both for 15 days; their blood was examined by biochemical and microbiological assays. Full tables of results are given.

The findings suggest that much of the previous work on PAS blood levels is irrelevant and that after 9–15 days' treatment with CaBPAS the serum has considerable tuberculostatic activity. Comparison with the results by microbiological method shows that whereas the results by both methods for CaBPAS are in fair agreement, in the sodium PAS group the microbiological method gave considerably lower results than the chemical. The authors suggest that the figure for PAS obtained by chemical method are augmented by the presence of biologically inert amines which are included by the usually accepted chemical tests. The results indicate that the blood levels produced by CaBPAS, though lower than those produced by sodium PAS, do not differ by such a large margin as has been previously reported. Further observations along these lines which are in progress will be awaited with great interest. If the results are confirmed this is a valuable piece of work.

F. H. Young

RISKA, N. **PAS Therapy with a Daily Unfractionated Dose.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, Nos. 1–2, 104–11.

This is a study of the advantages of a single large daily dose of PAS compared with the usual method of divided doses.

After a single large dose the concentration of PAS in the blood is temporarily much higher and LEHMANN (Libro de Actas de la XIII Conferencia Internacional contra la Tuberculosis, 1954, 591) has shown that the acetylation of PAS is inhibited by high blood concentrations. Especially in France the use of intravenous PAS in large doses has been popular for some years. Na PAS granules were given in 1 dose corresponding to 14–16 gm. of free PAS acid. Estimations of blood concentrations were made at 1½, 3½, and 5–7 hours after the PAS had been taken.

Na PAS in a dose corresponding to 17·5 gm. of free acid was given intravenously in the course of 1½–2 hours and blood estimations were made 1, 3½, and 5 hours after the end of the infusion.

The single dose was given to 78 patients and the intravenous dose to 18.

The results were as follows:

Highest PAS concentrations found in blood after unfractionated dose and after intravenous infusion.

Principle of treatment with NaPAS	gm. free PAS-acid	No. of subjects tested	Max. PAS concentration in mgm./100 ml. mean value
Unfractionated dose ...	>16	6	23·5
Unfractionated dose ...	16	57	28·4
Unfractionated dose ...	14	15	27·7
Intravenous infusion ...	17·5	18	32·3

After 5 hours the mean PAS concentration was still high in 10 of the 12 patients who had received 16 gm. in 1 dose orally, but in only 1 of those who had received the intravenous dose.

As regards tolerance, of the 56 patients who had both the oral methods, 23 reported no difference, 27 preferred the single, and 6 the divided dosage. Most of the 43 patients who could distinctly describe the side effects preferred the dose unfractionated. 17 who had taken the single dose reported nausea against 13 with the divided dose. 10 reported diarrhoea with a single dose against 24 with a divided dose. 6 reported poor appetite with a single dose against 15 with a divided dose. Otherwise the unpleasant symptoms were distributed fairly evenly between the 2 groups. *F. H. Young*

OLSEN, P. Z. & TORNING, K. **Psychological Side-Effects during Long-Term Ambulatory Chemotherapy with Isoniazid and PAS.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, Nos. 1/2, 89–103. [72 refs.]

This paper begins with a review of the reported toxic effects of isoniazid. It notes that the few reports on the psychological effects agree that no abnormality was discovered.

The object of the paper is to consider these effects on patients treated as ambulants with 4 mgm. isoniazid and 200 mgm. PAS per kgm. body weight. The period of treatment varied from 1 to 3 years.

52 patients were treated in a private clinic and were therefore more likely than the average to be engaged in mentally fatiguing work. 28 had psychological side effects: isoniazid was thought to be responsible in 18; in the other 10 other causes were at least contributory. The frequency was higher in women than men but not to a degree that was statistically significant. It was rare for the symptoms to occur when the patient was sheltered in hospital. The symptoms nearly always disappeared when isoniazid was discontinued. The common symptoms were fatigue, impairment of concentration and memory, depression and unbalanced state of mind. They usually appeared within the first few months of ambulatory treatment. A list of the 52 patients is given with details and a short additional note about those in whom the psychological symptoms appeared.

The work is discussed in an interesting way and it is freely acknowledged that a pre-treatment assessment is really necessary, and this will be done in the future. This preliminary report will be of great interest and will stimulate those who are responsible for this treatment to enquire more closely into its psychological effects. Most workers will probably be surprised by the results reported. *F. H. Young*

AAMODT, T. **Hypersensitivity Reactions to Streptomycin, Paraamino-Salicylic Acid and Isonicotinic Acid Hydrazine.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, No. 3, 195–202, 2 figs. [15 refs.]

"The frequency of hypersensitivity reactions in tuberculous patients treated with SM, PAS and INH is investigated and found to be fairly high in SM (5·9%) and PAS (4·5%) but low in INH (0·7%).

"Temperature rise and exanthemas were the most common symptoms, but many other symptoms were observed usually in connection with the two above mentioned.

"The sensitization time of SM was between 1 (previously treated patients) and 150 days, of PAS between 2 and 180 days and 2 patients with INH-hypersensitivity got their symptoms after 28 and 30 days.

"In SM and PAS-hypersensitivity intracutaneous tests were found to be of value.

"Desensitization without steroid protection is recommended as a simple and safe procedure. In this material it is found to be successful in most cases."

YAMAMOTO, K. & KAKIMOTO, S. **Studies on the Antitubercular Compounds (XVII). With special reference to the Development of Resistance to the PAS Salt of INAH in** *Mycobacterium tuberculosis*. *Japanese J. Tuberculosis.* 1959, Mar., v. 7, No. 1, 45–8, 1 fig.

H37Rv growing in Kirchner medium containing serum developed a 200-fold increase in resistance to isoniazid during 8 serial passages, and to PAS during 10 passages, but 21 passages were necessary before the bacilli became resistant to the PAS salt of isoniazid (PAIN) and after 22 passages in a mixture of PAS and isoniazid in equal molar concentrations the resistance had increased only 10-fold. Partial cross resistance to PAIN was shown by both the isoniazid-resistant and PAS-resistant variants. The variant resistant to PAIN was resistant to both isoniazid and PAS whereas the one showing partial resistance to the PAS mixture was resistant to isoniazid and PAIN but not to PAS.

The authors maintain that these results support their contention that PAIN acts differently from a simple mixture of PAS and isoniazid and that it in fact behaves as a new compound. Judging, however, from clinical findings and from the present observations, PAIN cannot replace combined therapy with isoniazid and PAS.

S. R. M. Bushby

MOORE, T. & SHARMAN, I. M. **Nutritional Studies of Isoniazid in Rats deficient in Vitamin E.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 223–31, 2 figs. [23 refs.]

One of the theories advanced to explain the antituberculous activity of isoniazid is that it acts through its antioxidant activity, and this theory is supported by the fact that isoniazid has been shown to replace vitamin E in the diet of rats. The drug has been shown by BERGEL to prevent the brown coloration of the uterus of vitamin E deficient rats and the brown coloration of the body-fat when the deficiency was associated with the administration of large quantities of cod-liver oil. It also prevented the degeneration of the testes. In the present experiments the authors attempted to obtain further evidence of this action of isoniazid.

Rats were fed from the time of weaning on a diet containing lard as the only source of fat and to this was added isoniazid or nicotinamide. Some of the rats of the isoniazid groups were also given cod-liver oil.

Examination of the animals after 100–168 days showed that the isoniazid had a reversal effect against some of the lesions of vitamin E deficiency; it prevented the rapid post-mortem histolysis of the kidneys and the mottling of the incisor teeth, and it also lessened the brown coloration of the uterus but it had no effect on the degeneration of the testes or on the increased lysis *in vitro* of the red cells by dialuric acid. In the experiments in which the cod-liver oil was given the brown colour of the body-fat was also reduced. Nicotinamide also prevented some of these changes.

The authors therefore conclude that in general isoniazid reduces the effects of vitamin E deficiency and if it can be accepted that the brown coloration is a sign of peroxidative changes it seems logical to accept that isoniazid acts as an antioxidant. However, methylene blue is a much more effective substitute for vitamin E, so unless this dye has unsuspected chemotherapeutic properties in tuberculosis, it seems unlikely that the value of isoniazid as an antituberculous drug depends on its ability to act as an antioxidant. *S. R. M. Bushby*

NATHAN, A. **Streptovaricin and Isoniazid in the Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1959, Sept., v. 80, No. 3, 424–5.

"On the basis of an eight-month treatment period of 40 patients with streptovaricin and isoniazid, it is concluded that streptovaricin does not delay the emergence of tubercle bacilli resistant to isoniazid. Moreover, no evidence was found that streptovaricin at this dosage, along with isoniazid offers more in therapeutic efficiency than might have been achieved from isoniazid alone. In one-fifth of the cases, toxicity due to streptovaricin was severe enough to warrant discontinuance of the drug."

RILEY, E. A., SIMPSON, D. G. & BOWEN, J. F. **Streptovaricin alone in the Treatment of Active Pulmonary Tuberculosis. A Short-Term Clinical Study.** *Amer. Rev. Respiratory Dis.* 1959, Sept., v. 80, No. 3, 426–30, 2 figs.

"Among 28 patients with moderately or far advanced pulmonary tuberculosis started on streptovaricin therapy, 20 completed a four-month course of treatment. Three patients left the hospital before treatment was completed. The drug was discontinued in 2 because of gastrointestinal disturbances, in 2 because of roentgenographic worsening, and in one because of the appearance of lymphocytes in the cerebrospinal fluid. The sputum of 5 patients became negative for tubercle bacilli on culture at the end of four months. No significant roentgenographic change was observed in 3 patients; slight clearing took place in 8; and moderate improvement was noted in 8 patients. Extension of an area of pre-existing disease was noted in one. Except for the 2 patients with progressive disease, symptomatic improvement was noted in the whole group. Side effects were limited to gastrointestinal disturbances. Studies of the emergence of bacillary resistance to streptovaricin showed that varying degrees of resistance developed in all patients.

"Further clinical studies should be undertaken with streptovaricin with a more purified form of the drug than is now available, and additional studies in combination with another drug of known antituberculous activity would also seem indicated. A daily dose of 10 gm. of streptovaricin is as well tolerated as 5 gm., but the results of this preliminary study in a small group of patients do not suggest that the therapeutic effect of this high-dose schedule is superior to that of the low-dose schedule."

DES PREZ, R., JORDAHL, C., DEUSCHLE, K., MUSCHENHEIM, C. & MCDERMOTT, W. **Streptovaricin and Isoniazid in the Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1959, Sept., v. 80, No. 3, 431–3. [Refs. in footnotes.]

"A group of 55 previously untreated patients with moderately advanced and far advanced tuberculosis were treated with streptovaricin and isoniazid. At the six-month evaluation point 92 per cent had achieved substantial roentgenographic improvement, 51 per cent were judged to have closed their cavities, and reversal of infectiousness had occurred in 67 per cent. These results do not differ significantly from those obtained in a similar group of patients treated with isoniazid alone. With respect to reversal of infectiousness, the present results are inferior to those obtained with isoniazid-pyrazinamide. It is concluded that at the dosage used the combination of streptovaricin and isoniazid is no more effective than isoniazid alone."

PAUL, A. T. S. & URAGODA, C. G. **Surgery of Tuberculosis in Ceylon. A Review of Two Hundred and Fifty Cases.** *Tubercle.* 1959, Apr., v. 40, No. 2, 93–8.

This paper reports 250 patients who underwent surgical treatment for pulmonary tuberculosis in Ceylon in 1952–56. 14 died as the result of surgery. The main operations were thoracoplasty 115 (3 deaths), lobectomy 73 (3 deaths), pneumonectomy 30 (7 deaths).

The thoracoplasty results were considered satisfactory considering the extensive disease present in many patients. A full course of antimicrobial drugs was given before and after operation. 15% of patients were resistant to at least 1 drug at the time of operation, and, rather to the surprise of the authors, spread was not more common after operation. Bronchopleural fistula occurred in 14% of the resections. A satisfactory complete follow up could not be arranged. [The paper owes its interest to the fact that it refers to surgery in Ceylon rather than to any special surgical features.]

F. H. Young

LEWIS, A. G., Jr., DUNBAR, F. P., LASCHE, Eunice M., BOND, J. O., LERNER, E. N., WHARTON, D. J., HARDY, A. V. & DAVIES, R. **Chronic Pulmonary Disease due to Atypical Mycobacterial Infections.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 188–99. [32 refs.]

Since 1955 the Florida state tuberculosis hospitals have made a special study of patients excreting atypical acid-fast bacilli, and during 3 years 215 strains have been identified; the present report is concerned with only the first 100 cases.

All these strains were capable of growing at room temperature and none grew in tight "cords"; they were all catalase-positive. 7 of the strains were photochromogens, 78 were non-chromogens, producing buff or yellowish colonies in either light or darkness, and 15 were scotochromogens, 2 being of the red-orange type and 13 of the presumably non-pathogenic yellow-orange variety. The rate of growth on subculture ranged from 6 to 28 days for the photochromogens, from 6 to 42 days for the non-chromogens and from 6 to 28 days for the scotochromogens. None of the strains produced progressive disease in guineapigs, but all the photochromogens, half of the non-chromogens and none of the scotochromogens were pathogenic to mice.

Sensitivity tests were done on 46 strains before starting chemotherapy. Most of the strains showed some susceptibility to 10 μgm. streptomycin per ml. Almost half of the scotochromogens and the photochromogens showed some susceptibility to 1 μgm. isoniazid per ml. and to 10 μgm. PAS per ml.; most of the non-chromogens were completely resistant to these drugs. All, except 3, of the strains were at least partially sensitive to 1 μgm. streptovaricin per ml., and most were partially susceptible to 20 μgm. cycloserine per ml. Most of the strains were resistant to 10 μgm. viomycin per ml. but there was some degree of susceptibility to kanamycin and sulphisoxazole.

In the histories of 82 of the patients tubercle bacilli had not been isolated with certainty though there was doubt in 21; in 6 patients the atypical bacilli were isolated once only, but in 55 they were isolated on 2 or more occasions, sometimes more than 10 times. Most of these infections were in older white males and in the majority the onset was insidious, although in 11 patients it had been acute; a few were asymptomatic. The physical signs differed in no way from those of tuberculosis and most of the patients were tuberculin-positive although 11 of 61 patients whose bacilli were non-chromogenic were negative to 0·0001 mgm. PPD.

Treatment consisting of the administration of isoniazid and a variety of other antituberculous drugs, as well as resectional surgery when feasible, was relatively unsatisfactory. 10% of the patients have died and 48% are still excreting the bacilli. The treatment recommended is rest, administration of isoniazid with 2 or more drugs and surgical removal of residual foci of disease or cavities.

S. R. M. Bushby

VENEREAL DISEASES

LAUZIER, J. & LAFAGE, D. Récapitulation des renseignements recueillis au cours de l'année 1958 concernant les statistiques des maladies vénériennes **[Recapitulation of Information received during 1958 concerning Statistics of Venereal Diseases]** *Bull. Inst. Nat. Hyg.* Paris. 1959, July–Aug., v. 14, No. 4, 739–66, 2 maps & 7 graphs.

A short introduction sets out the headings of reported cases of venereal disease, of the activities of dispensaries and of the percentage of cases of syphilis found by prenuptial, pre- and post-natal examinations, prisoners, foreign workers and those applying voluntarily for treatment.

Results are set out in 20 tables, 7 graphs and 2 maps.

In 1958, 14,611 cases of gonorrhoea and 1,461 of syphilis were reported; the incidence per 100,000 was 32·9 for gonorrhoea and 3·3 for syphilis; contagious syphilis fell from about 16,000 cases in 1946 to about 2,000 in 1951 and then remained fairly steady till 1958; much the same applied to gonorrhoea. Details are given of numbers of reported cases of syphilis, gonorrhoea and chancroid each year since 1945 and of those attending dispensaries; of the various categories of persons examined; of the monthly numbers reported during 1958; of the different sources of infection; of the different reporting agencies and of age-groups affected for the 3 venereal diseases.

Such a mass of statistics cannot be given in an abstract; those interested should study the original.

What is clear is that venereal diseases fell rapidly after the war and then remained steady, that soft chancre is now uncommon, that prostitutes still present a big problem in France, and that serum tests of those about to marry and of pregnant women and new born babies are well worth while. *T. E. Osmond*

KLINE, B. S. **Discussion of the Report of the 1956–1957 Serology Evaluation and Research Assembly.** *Amer. J. Clin. Path.* 1959, Aug., v. 32, No. 2, 134–9, 1 fig.

38 laboratories participated in this evaluation, performing 18 non-treponemal, 13 treponemal [presumably this means employing an antigen made from spirochaetes] and 7 Reiter treponeme protein tests for syphilis.

Sera included: presumed normal 346, diseases other than syphilis 74, primary syphilis untreated 130, secondary syphilis untreated 91, treated early syphilis 51, treated late syphilis 232, biological false positive 117 and biological false positive (clinical impression) 110. Results are set out in 4 tables and 1 figure. From these it appears that the Kline slide flocculation test with synthetic lecithin ranked first for combined sensitivity and specificity, ninth in the normal and untreated early syphilis specimens and second in the presumed normal and untreated secondary syphilis specimens.

Treponemal and Reiter treponeme protein tests do not seem superior to the others in distinguishing between true and biological false positive tests. [There are so many abbreviations such as Army CSF, Kahn TF, Kline NL CSF, Kolmer S1 LCF and VDRL CTF that it is not easy to understand the tables; the reader who is interested is invited to examine these tables in the original.] *T. E. Osmond*

KRAG, P. & BENTZON, M. W. **Third International Reference Preparation of Cardiolipin with special reference to its Use in Improved Serological Tests for Treponematoses.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1193–200. [10 refs.]

This article is purely of academic interest. The preparation of cardiolipin was patented in 1947 and it was intended that both this and lecithin should be standardized by comparison with reference preparations. The first reference preparation of cardiolipin was established by the WHO expert committee in 1951 and the second in 1953. The present article deals with the third reference preparation; the assay of this was carried out in 4 laboratories—1 each in France and Denmark and 2 in the U.S.A.; each laboratory tested 32 reactive sera and 200 non-reactive sera. Results are shown in the text and in 4 tables from which it can be seen that both with slide and complement-fixation tests the third preparation of cardiolipin was acceptable as a replacement for the second international reference preparation. Differences from laboratory to laboratory were largely such as would be expected from the selection of sera for testing; the different antigens had practically the same reactivity in each of the 4 laboratories. *T. E. Osmond*

LAURELL, Anna B. & HEDERSTEDT, B. **Fractionation of TPI Antibodies and Wassermann Reagins.** *Acta Path. et Microb. Scandinavica.* 1958, v. 44, No. 1, 88–91, 1 fig.

REALMUTO, A. & CENSUALES, S. Accertamento sierologico della sifilide su 41,675 donatori volontari di sangue. **[Serological Survey for Syphilis on 41,675 Voluntary Blood Donors]** *Ann. d. San. Pubblica.* Rome. 1959, May–June, v. 20, No. 3, 515–25. [22 refs.] English summary.

The authors quote COFFARI and MARCOZZI who have studied the incidence of venereal disease during 1947–51 and found that there was a progressive decline in recent syphilis but also an increase in the number of individuals who were not aware of being infected [this *Bulletin*, 1955, v. 30, 587].

The present survey covered the three years 1955–57 and the 41,675 blood donors were citizens of Rome, aged between 21 and 50, representative of a wide range of social classes, in a normal state of health and without any known history of syphilis. Any volunteers with a history of infective hepatitis, malaria, brucellosis, tuberculosis, epilepsy, skin or heart disease were not accepted and are not in this group of blood donors.

10 cc. samples of blood were taken from each donor and tested for (a) complement fixation with cardiolipin,

(b) complement fixation with a suspension of the Reiter strain of spirochaete, (c) Kahn flocculation and (d) VDRL slide microflocculation test. The authors of this survey outline the technique which they followed for these tests.

Samples which gave a positive or doubtful complement fixation test were then tested quantitatively by Kolmer's technique (incubation for 12–14 hours at 4°C., with 2 units of complement). Known positive and negative sera were used as controls in each case.

Among the 41,675 specimens of serum, 719 were found to be positive to one or more tests. A proportion of positive samples were subjected further to the immobilization test of Nelson and Mayer, which is particularly sensitive and specific.

As a result of this survey it is estimated that some 1·4% of these blood donors had a latent syphilitic infection. *J. Cauchi*

MILLER, J. N., BOAK, Ruth A. & CARPENTER, C. M. **A Stable Antigen for the *Treponema pallidum* Immune Adherence (TPIA) Test for Syphilis.** *Amer. J. Clin. Path.* 1959, Aug., v. 32, No. 2, 187–91.

The preparation of this antigen is somewhat complicated but is carried out on the usual lines; rabbit syphilomas were cut up and placed in sodium citrate solution; this was shaken, centrifuged to remove debris and then recentrifuged at high speed and the sediment resuspended in buffered saline and adjusted to contain 8–13 spirochaetes per field.

3 antigens were prepared (1) unheated, (2) heated at 60°C. for 2 hours, (3) the same as (2) but heated a second time at 100°C. for 1 hour. Human group O blood cells and human or guineapig complement were employed. 9 tubes were used in the test including controls; after addition of antigen, Hanks salt solution and serum, primary incubation was carried out in a water bath at 37°C., complement and red cells were then added and followed by further incubation at 37°C.; the tubes were then centrifuged, the supernatant removed and the number of spirochaetes in each of 20 fields counted.

Disappearance of 25% or less of spirochaetes was recorded as negative, of 26–49% as doubtful and of more than 50% as positive.

The unheated antigen (1) proved poorly reactive, antigen (2) remained stable for 3 months and antigen (3) for 4 months.

When TPIA and TPI tests were compared there was complete agreement on 26 normal sera, 88% agreement on 25 sera from patients with early syphilis and 98% agreement on 51 sera from patients with no history of syphilis but with positive serum tests; the TPIA seemed the more sensitive in cases of early syphilis and gave higher titres on known syphilitic sera. All antigens contained Merthiolate 1/10,000 as a preservative; antigens heated twice proved more sensitive than those heated once.

For full details of preparation of antigen and the setting up of the test the original should be consulted. *T. E. Osmond*

CENSUALES, S. & GAROFALO, V. Anticorpi antitreponemici nella sifilide umana svelati con la reazione di fluorescenza. **[The Demonstration of Antibodies against Treponemes in Human Syphilis by the Fluorescence reaction]** *Riv. Istituto Sieroterap. Ital.* 1959, May–June, v. 34, No. 3, 161–7. [19 refs. English summary.

The authors describe their experience with a test originally described by DEACON, *et al.* [see this *Bulletin*, 1958, v. 33, 461]. A drop of treponeme suspension is deposited on a slide so that there are 5 to 10 micro-organisms per field. After drying in air the slide is immersed for 10 minutes in acetone to remove any background fluorescence. About 0·03 ml of patient's serum diluted 1 in 5 is dropped on the dried preparation and allowed to act for 30 minutes. The preparation is then washed in a buffer solution and anti-human-globulin serum which had been rendered fluorescent by conjugation with isocyanate of fluorescein, diluted 1 in 5, is dropped and allowed to act for 30 minutes at 37°C. After 2 washings in buffer solution, a drop of a mixture of 9 parts glycerin and 1 part buffer solution is applied and a cover slip is put on. Examination is carried out by dark-ground methods. The treponemes which have reacted with serum from syphilitic cases show a yellowish-green fluorescence of varying intensity.

On a 100 cases 4 reactions, the fluorescence reaction the TPI test, the Reiter protein complement-fixation test and the cardiolipin complement-fixation test, were compared, taking the TPI test as the standard of positivity. The most important finding was the agreement between the TPI and the fluorescence tests. The 4 tests were positive in 38 cases, TPI and fluorescence tests were positive in 16 other cases. The fluorescence test has the advantage that it needs less complicated apparatus than the TPI test, and anaerobic conditions are not necessary at any stage. The antigen consists of killed treponemes and this is more convenient than the TPI antigen. More experience is needed to appreciate fluorescence than treponeme immobilization; the possibility of expressing the reacting power of sera in terms of percentages of immobilization is also an advantage of the TPI test. *E. Agius*

MONTGOMERY, C. H. & KNOX, J. M. **Antibiotics other than Penicillin in the Treatment of Syphilis.** *New England J. of Med.* 1959, Aug. 6, v. 261, No. 6, 277–80. [54 refs.]

This article purports to be a review of the English [? American] literature on antibiotics, other than penicillin, in the treatment of syphilis.

Chlortetracycline—the various dosages recommended for early syphilis range round 40–70 gm. orally over 10–14 days; 200 mgm. intravenously daily for 15 days and 50 mgm. intramuscularly daily for 21 days combined with oral administration also give satisfactory results.

Chloramphenicol—the effective dosage appears to be 40–100 mgm. per kgm. body weight for about 8 days but for neuro-syphilis the period should be extended to 15 days.

Oxytetracycline—optimum dosage lies between 28

and 48 gm. over about 14 days; intravenous administration does not appear to have been very effective in the dosages used.

Of the other antibiotics bacitracin and subtilin were relatively ineffective; carbomycin 21 gm. in 10 days, erythromycin 12–20 gm. over 10–15 days, tetracycline 2 gm. daily for 12 days and novobiocin 30–120 mgm. per kgm. daily for 14 days have been reported on favourably.

None of the above is nearly as effective as penicillin and they should be reserved for penicillin-sensitive patients; in most of the case reports follow-up did not extend over a long enough period to assess adequately the value of the drugs, but their effects on spirochaetes and serum reactions were satisfactory.

T. E. Osmond

MONTGOMERY, C. H. & KNOX, J. M. **Erythromycin in the Treatment of Early Syphilis. A Preliminary Report.** *Arch. Dermat.* 1959, Aug., v. 80, No. 2, 205–9. [10 refs.]

After reporting some results of other workers in the treatment of syphilis by antibiotics other than penicillin these authors set out their results with erythromycin; 40 patients with early syphilis received erythromycin according to 1 of 4 schedules, (1) 250 mgm. orally 4 times a day for 10 days, (2) 500 mgm. 4 times a day for 5 days, (3) 750 mgm. 4 times a day for 3 days and (4) 250 mgm. intramuscularly daily for 10 days (erythromycin ethyl succinate). Results are set out in 4 tables showing rate of disappearance of spirochaetes and monthly blood tests. Under schedule (1) there were 19 successes and 2 failures, in schedule (2) 6 successes and 4 failures; in schedule (3) 1 success and 6 failures; in schedule (4) 2 successes.

In general, spirochaetes disappeared in 24–72 hours and serum tests tended to become negative reasonably quickly; side reactions were negligible until the dose was increased to 3 gm. daily.

It seems probable that either the period of treatment needs prolonging or that the intramuscular route should be used. *T. E. Osmond*

GJESSING, H. C. Tiltagende residivhyppighet etter penicillinbehandling (samme preparat og dose) for gonore. [**Increasing Frequency of Relapse after Penicillin Treatment (with Same Preparation and Dose) for Gonorrhoea**] *Tidsskr. f. d. Norske Laegeforening.* 1959, July 1, v. 79, Nos. 13/14, 829–31.

The tendency for the relapse rate to rise among patients treated with penicillin for gonorrhoea is indicated by the following figures supplied by the Oslo public health service. Between 4 November 1952 and 31 December 1954 the 305 patients given 300,000 units of procain penicillin G showed a relapse rate of 2–2·6%. Between 2 January 1955 and 24 November of the same year the 158 patients receiving the same dosage of penicillin showed a relapse rate of 7–9%. Between 26 October 1957 and 30 December of the same year the 28 patients who received the same dosage of penicillin showed a relapse rate of 8·6–11%. In the table giving these figures, relapses and re-infections are recorded separately instead of being lumped together, for Gjessing refuses to believe that they cannot be distinguished. In his opinion the attack which comes a week or two after the completion of treatment is a relapse, and the attack which comes later is more and more likely to represent a new infection the longer the interval between it and the completion of treatment.

His remedy for the growing relapse rate is to double the dosage of penicillin, and since January 1958 he has given 600,000 units. By May 1959 he had treated 255 males in this way, and he has had 5 relapses and 4 re-infections. For women he has for several years given 3 injections of 600,000 units, one injection every other day. He plans to stick to penicillin as his mainstay, not being tempted by streptomycin in whose wake also there is a rising tide of relapses. He does not recommend combining penicillin with streptomycin as by so doing it is difficult to learn to which of them the gonococcus has become resistant. *Claude Lillingston*

BARILE, M. F., VAN ZEE, G. K. & YAGUCHI, R. **The Occurrence of Failures in Penicillin-Treated Gonorrheal Urethritis. I. The Significance of L-Form Transformation of *Neisseria gonorrhoeae* to Penicillin Resistance.** *Antibiotic Med.* New York. 1959, Aug., v. 6, No. 8, 470–79, 5 figs. [44 refs.]

Of 165 patients with gonorrhoea treated with 600,000 units of procaine penicillin G daily for 3 days, 7 failed to respond; full case histories of these are given in the text; the penicillin tolerance of the gonococcus strains varied from 0·125 to 0·50 μ/ml. compared with 0·015 for a known sensitive strain. 1 patient was cured by 500 mgm. oxytetracycline 4 times a day for 5 days, 1 by the same amount of chlortetracycline, 1 by a further 5 days' treatment with penicillin and the other 4 by 250 mgm. of chloramphenicol 4 times daily for 5 days.

During the penicillin tolerance studies one strain of gonococcus produced L-forms when exposed to concentrations of penicillin ranging from 4 to 256 units per ml. of solid medium.

PPLO were recovered from 2 patients who were penicillin-resistant. There is no doubt that gonococci are tending to become penicillin-resistant as shown by the fact that 5 times as much is required nowadays to cure a patient as was needed in the early days of penicillin therapy.

6 figures show vesicular-pustular lesions on the prepuce and glans, a colony of PPLO, balanitis occurring with urethritis, intracellular gonococci, L-forms of gonococci and a muco-purulent discharge from the urethra; 1 table sets out the penicillin-resistance of 8 strains of gonococci. *T. E. Osmond*

HEDBERG, E. Den gonorrhoiska salpingitens prognos. [**The Prognosis for Gonorrheal Salpingitis**] *Svenska Läkartidningen.* 1959, Aug. 7, v. 56, No. 32, 2184–8.

At the Gynaecological Department of the Sahlgrenska Hospital in Gothenburg, gonorrhoeal salpingitis continues to provide a large share of its patients in spite

of improved prophylaxis and treatment. To throw more light on the prognosis for this condition in response to treatment with antibiotics, the practice has been adopted at this hospital during the past 2 years of submitting the patients to hystero-salpingography before they are discharged from it. The antibiotic treatment they received was in Hedberg's opinion adequate. It consisted of giving 800,000 international units of astracillin daily for 5 days after culture tests had confirmed the diagnosis. On completion of the antibiotic treatment and thenceforth at weekly intervals during the stay in hospital the culture tests were repeated. The hystero-salpingography was undertaken after the patients had become afebrile and symptom-free, and the sedimentation rate had become normal. Prophylactic treatment with antibiotics was given both before and after this examination which has not bee followed by any ill effects. The table concerned with thi examination in 70 cases takes into account the lengt of the interval between contracting the disease and re ceiving antibiotic treatment for it, as well as the fre quency with which the Fallopian tubes were obstructed Only in 14 cases were both of them obstructed whereas in 18 cases the obstruction was unilateral Conditions in this respect were normal in the remainin 38 cases. Hedberg concludes that the optimal benefit of specific treatment can be obtained only when th disease is caught early, and that "in the subacute an above all in the chronic stage of gonorrhoeal salpingitis sulphonamide and antibiotic treatment cannot b expected to effect any essential improvement".

Claude Lillingston

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

WOLFF, H. L. **The Filter Paper Method for shipping Blood Samples for Serological Examination.** *Trop. & Geograph. Med.* Amsterdam. 1958, Dec., v. 10, No. 4, 306–8.

The author writes with further experience of a filter paper method for transport of blood samples for serological tests which he described in an earlier paper (*Acta Leidensia* (*Scholae Med. Tropicae*), 1957, v. 26, 216).

He uses strips (0·5 × 10 cm.) of desk blotting paper which he finds more suitable than filter papers (which are commonly hardened): thick filter cardboard is also suitable. Blood from the ear lobe is absorbed on the strip in such a way that about one-fourth of the strip is unstained; this part is used for recording the patient's name. At least 2 strips are taken from each patient. The strips are dried by hanging them up by their clean ends away from insects; failing this, they are put in plates and covered with wire gauze. The dry strips are mailed to the laboratory in envelopes.

At the laboratory, the strips are placed in tubes with 0·75 ml. saline and after 20 minutes the fluid absorbed by the strip is expressed by pressing the strip against the wall of the tube with a glass rod as it is being removed. The fluid in the tube is estimated to contain antibodies comparable to a 1/60 to 1/90 dilution of serum. The fluid is suitable for all serological tests, but the initial dilution is a disadvantage as weakly positive reactions are missed; however, the antibodies found were identical with those found in serum samples tested in the ordinary way. The author has used the method for the Widal test, for complete and incomplete antibody estimations in brucellosis and for haemagglutination-inhibition tests with blood samples from mice infected with arthropod-borne viruses. Parallel tests were carried out on serum from the mice in the usual way. A table shows that the results compared well.

In complement-fixation tests, anticomplementary reaction occurred at first, but pre-treatment of the extracts with kaolin improved results. It was shown that the presence of kaolin did not produce non-specific absorption of the extracts. However, as complement-fixation titres tended to be low (less than 1/180) the author found it preferable in such tests to use serum dried on blotting paper instead of whole blood.

The method is economical, there is less chance of contamination than in the use of liquid serum and there is no danger of breakage.

H. J. O'D. Burke-Gaffney

LUPPI, A. Considerazioni statistiche sulla morbosità, nel Polesine, per il decennio 1946–55, del tifo, dei paratifi, delle brucellosi, della difterite e de'la poliomielite a.a. **[Morbidity of Certain Infectious Diseases in the Polesine 1946–1955]** *Riv. Italiana d'Igiene.* 1959, Jan.–Apr., v. 19, Nos. 1/4, 21–37, 8 figs. English summary.

This paper relates to the province of Rovigo in the Po-Adige delta. It covers an area of nearly half-a-million acres and has a population of about 350,000. No part lies more than 20 metres above sea level but in spite of this is traditionally divided into 3 areas; (a) Upper, (b) Middle, (c) Lower Polesine.

In the decennium 1946–1955 Lower Pol. had the highest incidence of enteric fever, though the numbers show a continued fall, and of brucellosis, the figures of which are surprisingly high [though no diagnostic criteria are given]. Next comes Middle Pol. and last Upper Pol. For diphtheria Middle and Lower Pol. are approximately equal, with Upper Pol. again the lowest, although the author cannot explain why. For Middle and Lower Pol. the number of cases of diphtheria per 1,000 was about 0·7 in 1954. After a fall from 1946 to 1951 the figures showed a considerable rise in all 3 areas in 1954; they fell by about half in 1955. For

poliomyelitis the differences in incidence in the 3 areas are less than for any of the others mentioned and after minor fluctuations between 1946 and 1952 there was a rise in 1953 which has been sustained.

The author concludes that those diseases which are most susceptible to changes in environmental conditions are decreasing but that brucellosis is increasing, for which he blames the nomadic flocks and their products. He considers that vaccination will reduce the incidence of poliomyelitis but that direct and drastic action is necessary as regards brucellosis. Much is hoped for from the new schemes of water supply which are now in progress. *W. K. Dunscombe*

INTERNAT. DIGEST HEALTH LEGISLATION. 1959, v. 10, No. 2, 193–255. [30 refs.] **Communicable Diseases in Schools. A Survey of Existing Legislation.**

"A study of recent legislation on communicable diseases in schools appeared in the *Digest* in 1952." (*Internat. Digest Health Legislation*, 1952, v. 4, 169). This work now appears in a revised form with omissions and additions. Its subject matter is arranged under the headings: legislation; exclusion measures; obligations of parents, teaching staff, and health services; measures relating to school staff; closure of schools; and conclusion. In a long appendix the practice adopted in many countries in respect of the periods of exclusion and other measures applicable to patients and contacts in communicable diseases in schools is tabulated.

There are very great differences between countries in the measures adopted for the prevention of spread of these diseases in schools and these differences are discussed at some length. Many studies on this prevention have appeared especially during recent years yet "it would seem that there is too much disparity in the data available to permit the establishment of uniform measures against the diseases in question". The resulting differences of opinion together with "the slowness with which new principles are introduced into the health legislation of various countries" are the reasons for the differences in legislative provisions. Regulations should be adapted and amended "more rapidly so that only measures justified by experience and recent scientific knowledge are retained".

In the conclusion to this admirable study there is the sentence—"It is surprising to find that there is virtually no uniformity whatever in the measures prescribed for dealing with the occurrence in schools of diseases whose epidemiology, evolution, and method of spread are well-known. The only positive element that emerges from this study, as compared with the conclusions drawn from the preceding work in 1952, is that there is a tendency to reduce the stringency of the exclusion measures relating to both patients and contacts." *M. E. Delafield*

MCDERMOTT, W. **Inapparent Infection. Relation of Latent and Dormant Infections to Microbial Persistence.** *Pub. Health Rep.* Wash. 1959, June, v. 74, No. 6, 485–99, 2 figs. [22 refs.]

"*Microbial Persistence*" denotes the survival of microbes in the tissues after antimicrobial therapy. Such persisting microbes cannot multiply but are not permanently incapacitated: they are in a latent or dormant state.

"*Latent Infections*" are inferred when frank disease appears in tissues from which adequate techniques fail to demonstrate organisms. Latency is an extreme of microbial adaptation and is accomplished by considerable morphological and physiological changes.

In "*Dormant Infections*" organisms are readily demonstrable in small numbers yet do not produce disease: the normal flora with pathogenic tendencies and organisms of healing wounds and carrier states are included. Re-emergence requires little microbial activity, merely inadequacy of host defences. Inapparent infections are most commonly due to dormancy: latency is less usual (or less detected). Latency is dealt with from two points of view.

I. *Latent Infections emerging as frank disease*

Rats known to be resistant to *Corynebacterium pseudotuberculosis-muris* and to be free from detectable quantities of the organism in their lungs succumb to it endogenously when given cortisone. Moniliasis, herpes simplex, and lysogenic phage are instances of emergence of latent infections.

II. *Conversion of frank disease to latency*

Human (but not bovine) tubercle infections of mice can be made truly latent by treatment with pyrazinamide and isoniazid. Re-emergence of frank disease in $\frac{1}{3}$ of cases by the 90th day after cessation of treatment shows that the organisms have not merely been eliminated.

Microbial persistence is thought to be due to drug indifference rather than to genotypic drug resistance or inadequate dosage: it is thought to be an adaptive response to environmental change.

In persistence due to latency the evidence in favour of a major morphological change is:—

(1) Penicillin can produce bacterial protoplasts.

(2) The genera considered—*Corynebacterium* and *Mycobacterium*—undergo considerable pleomorphism.

(3) The pyrazinamide- and isoniazid-induced latency mentioned above requires very carefully controlled conditions for its success. It is a highly specific adaptive process resulting in the disappearance and presumptive morphological change of the organisms.

Microbial persistence is not commonly due to latency, only the pyrazinamide and isoniazid system and perhaps latency in *Treponema pallidum* being examples. Among those bacteria which are not immediately destroyed by antibiotics and are not genotypically resistant, dormancy is a more common reason for persistence. It has been shown by giving antibiotics in the early stages of syphilis, malaria, scrub typhus, tuberculosis, and Q fever that eradication is impossible if drug indifference is present from the start: such drug-modified infections may not give an immune response.

Latent infections may damage tissues and the lightning pains of syphilis and their response to penicillin is quoted.

In conclusion grave illness is stated to be due less to genotypic resistance or antimicrobial underdosage and more to organisms which never were truly sensitive. These persist in the dormant or latent state and emerge

as frank infection when their environment is disturbed by injudicious therapy. *Stewart Fletcher*

HOSPITAL AND OTHER CROSS INFECTIONS

COLES, R. B. **Report on the Use of a Notification System of Staphylococcal Sepsis in a General Hospital.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Aug., v. 18, 132–5.

For the recording of staphylococcal sepsis, each ward is provided with a "sepsis book" in which are entered details of any patients who develop any clinically manifest infection while in hospital. These entries are made on the day that the disease is noted, by the ward sister, and are subsequently verified by the medical staff. The sepsis records are examined weekly by the hospital sepsis officer who prepares a forecast from the statistics of the incidence of sepsis in the wards each week. He correlates this information with laboratory reports. [Strictly, it is not possible to quote incidence rates without a knowledge of the population at risk.] The rates are communicated to the medical staff at appropriate intervals. It is thought that this notification system has already proved its worth in enabling rapid action to be taken to limit outbreaks of staphylococcal sepsis. *R. E. O. Williams*

See also p. 68, KOCH, KASTENSEN & RESNICK, **Report on Commonly Occurring Phage Patterns in a Hospital in which Staphylococcal Infections are Endemic.**

RILEY, I. D., HUNTER, Janet L., MACWILLIAM, P. K. & COUTTS, Vera C. **Infection and Breast Feeding in the Newborn at Home and in Hospital.** *Scottish Med. J.* Glasgow. 1959, Sept., v. 4, No. 9, 451–4. [19 refs.]

"Eighty-six hospital-born and fifty-four home-born infants were visited when 8 weeks old. Enquiry was made about infection and breast feeding. The incidence of infection was 18 per cent in hospital cases and 20 per cent in home cases. The incidence of breast feeding in both groups was less than 10 per cent."

WATT, J., WEGMAN, M. E., BROWN, O. W., SCHLIESSMANN, D. J., MAUPIN, Elizabeth & HEMPHILL, Emmarie C. **Salmonellosis in a Premature Nursery unaccompanied by Diarrheal Disease.** *Pediatrics.* Springfield, Ill. 1958, Oct., v. 22, No. 4, Pt. 1, 689–705, 2 figs.

This is a detailed epidemiological, bacteriological, and clinical account of an outbreak of symptomless Salmonella Tennessee infection in a nursery for premature infants in New Orleans. The infection was introduced simultaneously by 6 healthy premature infants transferred for routine reasons from a hospital. The infection with this potential pathogen was found in the course of routine bacteriological examination of the stools on admission. During the next few days 5 other infants in the nursery became infected with the organism, again without symptoms, and then after an interval of 28 days, the infection was detected again in 23 infants over the course of some 3 months.

Although the infection was apparently introduced from the transferring hospital, the original source could not be determined. Within the nursery the feeds, contact with other patients, and infected animals could all be eliminated as modes of spread, and cultures of the stools of nurses and attendants were all negative. Infection of the air of the nursery was demonstrated by the slit sampler method in 1 sample out of 455 examined, and in 1 swab of the air filters out of 30 examined. Among 232 cultures made from the equipment in the affected infants' units, 6% were positive for Salm. Tennessee, and 2·4% of 82 cultures were positive in empty infants' units cleaned and ready for new occupants. The nurses' hands were found infected in 0·8% of 130 cultures taken, including the hands of one nurse immediately after washing. The bacteriological evidence suggested that increase in spread was associated with decrease in amount of nursing care, particularly defective hand washing.

H. Stanley Banks

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus, Streptococcus, Neisseria, Others.*

STAHLMAN, Mildred T. & DENNY, F. W., Jr. **The Prophylaxis of Streptococcal Infections in Patients with Rheumatic Fever. A Comparison between Sulfadiazine and Erythromycin.** *J. Dis. Children.* Chicago. 1959, July, v. 98, No. 1, 66–71. [20 refs.]

The authors feel that neither sulphadiazine nor penicillin is an ideal drug in the prophylaxis of streptococcal infections and rheumatic relapses: sulphadiazine does not eradicate streptococci from the pharynx in acute conditions and both drugs cause some toxic effects. Erythromycin by mouth, 100 mgm. night and morning was therefore tried. 50 children were treated, 25 having sulphadiazine 0·5 gm. night and morning, the other 25 having erythromycin. The patients were treated for an average period of 19½ months. In the sulphadiazine group 1 patient had a rheumatic relapse and 7 had positive throat cultures for group A haemolytic streptococci: in the erythromycin group there were no rheumatic incidents and only 1 patient had a positive throat culture. There were no untoward reactions to either drug. *A. B. Christie*

KAUHTIO, J. & JANSSON, E. **Acute Bacterial Meningitis in Adults. Review of 95 Cases treated in 1937–56 at the Aurora Hospital.** *Ann. Med. Intern. Fenniae.* Helsinki. 1959, v. 48, No. 1, 33–43, 2 figs. [19 refs.]

The great majority of cases of acute bacterial meningitis occur in infants and young children. This report on the condition in 95 adults in a hospital in

Helsinki has therefore only some scarcity value, which is diminished by the time factor, since treatment was revolutionized during the 20-year period over which the cases were collected.

Meningococcal meningitis tended to affect adults under 40 years of age, whereas two-thirds of the pneumococcal subjects were over 40. Pneumococcal meningitis appeared to be the more common form in the latter 10 years of the period, and the relative disappearance of the meningococcal form during this period was thought to be due to the general use of antibiotics in almost every febrile illness. There were 3 cases of permanent deafness among the 59 cases known or assumed to have been caused by the meningococcus—approximately 5%. [This is similar to the incidence in BANKS's series of 706 cases of all ages (this *Bulletin*, 1949, v. 24, 387) in which the age incidence of deafness was found to be spread almost uniformly from infancy to old age.]

Among the 12 patients with pneumococcal meningitis treated in the first 10 years, 11 died, and among the 17 treated in the second 10 years, 3 died. The credit for the difference is rightly given to penicillin treatment in large doses (12 million units/day) given mainly intramuscularly; intrathecal treatment of meningitis is not considered necessary. Bacterial meningitis in adults caused by other organisms is rare: there were 7 cases in 20 years, with 4 recoveries.

The authors recommend lumbar puncture for diagnosis in every suspected case of meningitis, but antibiotics should not be given unless there are clear indications that the cause is bacterial.

H. Stanley Banks

BACTERIAL INFECTIONS

The order in this section is:—*General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.*

LAUTROP, H. **Observations on Parapertussis in Denmark, 1950–1957.** *Acta Path. et Microb. Scandinavica.* 1958, v. 43, No. 3, 255–66, 2 figs. [21 refs.]

"During the course of seven years (1950–1957), 1040 cases of parapertussis have been demonstrated bacteriologically in Denmark. It is estimated that the total number of cases actually occurring during that period was between 200,000 and 300,000—a figure which suggests that parapertussis and pertussis occur with about equal frequency.

"The time-distribution of the confirmed cases shows that parapertussis is endemic and reaches epidemic proportions at intervals of a few years. The epidemic waves of pertussis and parapertussis occurred independently of each other.

"About equal frequency of pertussis and parapertussis among the population would mean that most children contract both infections. This assumption is borne out by a follow-up study of a group of 127 children: besides a bacteriologically confirmed diagnosis of parapertussis in all children, a clinical (43 cases), or bacteriological (30 cases) diagnosis of pertussis has been made in 73 (or 57·5 per cent) of the children in the group. It is shown that the figure would have been still higher but for the influence of vaccination and various other factors.

"Including the 30 mentioned above, a total of 79 cases are now on record in which a bacteriologically confirmed diagnosis of both pertussis and parapertussis, occurring simultaneously or successively, has been made."

NICHOLSON, C. C. **Observations on the Incidence, Aetiology and Prevention of Typhoid Fever and the Diarrhoeal Diseases in British Guiana.** *Caribbean Med. J.* 1957, v. 19, Nos. 1/2, 24–39. [13 refs.]

With a population of less than half a million there are seldom fewer than 500 cases of typhoid fever in British Guiana every year according to this report, but whether these are bacteriologically confirmed cases is by no means clear. Indeed this paper provides very little exact information about typhoid fever or the diarrhoeal diseases in British Guiana except that the incidence is "very high". "Diarrhoeal diseases" cover gastro-enteritis, colitis, bacillary and amoebic dysentery, and the death-rate due to this group of diseases in 1952 for example was 154·7 per 100,000 of the population. Most of the tables appear to have been prepared for one purpose; to show the very high incidence of these two groups of diseases in British Guiana as compared with many other countries of the Americas.

H. J. Bensted

KHO LIEN-KENG & ODANG, O. **The Bone Marrow Picture of Typhoid Fever in Childhood.** *J. Trop. Pediatrics.* London. 1959, Sept., v. 5, No. 2, 35–44, 7 figs. [26 refs.]

The bone marrow was studied in 50 Indonesian children suffering from typhoid fever, usually during the second week of the disease. There was increased granulopoietic activity, except for the eosinophil series which showed a notable arrest at the metamyelocyte stage. There was diminished erythroblastic activity, and a high myeloid/erythroid ratio. Cells of the reticulo-endothelial system were hyperactive, and a frequent finding was phagocytosis of red cells, granulocytes, and platelets by macrophages. All these changes accounted satisfactorily for the well-recognized peripheral blood count in typhoid fever.

3 case-histories are given.

Alan B. Raper

KOSANOVITCH-CHETKOVITCH, D., KOSTITCH-VUJACHICH, A. & SIMONOVICH, B. Étude critique de l'électrophorégramme dans la fièvre typhoïde. **[Critical Study of Serum Electrophoresis in Typhoid Fever]** *Rev. d'Immunologie.* 1959, Apr.–June, v. 23, No. 3, 181–9. 3 figs.

Electrophoretic studies on 34 patients suffering from typhoid fever showed a fairly consistent lowering of albumin and a rise in alpha 2 globulin, beta and gamma globulin. There was no difference in the findings in mild or in severe complicated cases nor were

the changes different from those found in other febrile illnesses. In children gamma globulin showed a sharp rise followed eventually by a fall whereas in adults there was no marked oscillation of titre. In many of the cases, the Widal test remained negative although the gamma globulin rose and the authors refer to the possibility that early treatment with chloramphenicol may suppress antibody production. *A. B. Christie*

KOSANOVITCH-CHETKOVITCH, D., KOSTITCH-VUJACHICH, A. & SIMONOVICH, B. Influence des rechutes de la fièvre typhoïde sur le niveau de la globuline gamma. [**Influence of Relapse in Typhoid Fever on the Level of Gamma Globulin**] *Rev. d'Immunologie.* 1959, Apr.–June, v. 23, No. 3, 190–95, 2 figs. [16 refs.]

A rise of antibody can be demonstrated after the second and subsequent injections of typhoid vaccine and the authors decided to study whether a relapse in typhoid fever might show a similar rise. Relapses have become much commoner since chloramphenicol became available: the authors quote one series, before chloramphenicol, of 760 cases with a relapse rate of 8·9% and a series of 333 cases, with chloramphenicol, with a relapse rate of 26·7%. In the series of 67 cases on which the present study is based the relapse rate was 40%, 54% in infants and 32·5% in adults. Electrophoretic studies were carried out on the serum of 33 cases. Raised gamma globulin was always present in the serum before a relapse and in cases without relapse so that there was no way of forecasting which cases would and which would not have a relapse. Relapses took place even where there was a very high gamma globulin level. Relapses did not cause any alteration in the electrophoretic curves except that return to normal was delayed because of the longer illness.

A. B. Christie

i. TURNER, R. **Vaccination against Typhoid Fever.** *South African Med. J.* 1959, Aug. 1, v. 33, No. 31, 639–40. [11 refs.]

ii. ——. **The Role of the Laboratory in the Diagnosis and Control of Typhoid Fever.** *Ibid.*, 643–7.

iii. SMITH, L. S. **The Laboratory Diagnosis of Typhoid Fever. An Outline of the Methods used at the Government Pathological Laboratory, Cape Town.** *Ibid.*, 647–9.

iv. LANGERMAN, R. M. **Typhoid Fever: Preventive Measures.** *Ibid.*, 649–50.

i. This is a very brief and incomplete consideration of the value of vaccines for the prevention of typhoid fever. It is only partially documented but the author mentions an experience of very considerable interest although, in the absence of exact details, its importance cannot be assessed. In 1943 two groups of individuals, inoculated and uninoculated, were equally exposed to infection from a typhoid-contaminated water supply. The actual numbers in each group are not given but it is stated that the incidence of typhoid among the inoculated was 1·1% whereas the incidence in the uninoculated was 7·0%.

The field trials of the alcoholized and the phenolized TAB vaccines in 1954–55 in Yugoslavia are briefly mentioned. Although Grasset's endotoxoid vaccine has never been subjected to controlled field trials it is considered to be as effective as the ordinary phenolized TAB vaccine. While vaccination against typhoid can be recommended for the Armed Forces and others at special risk it is not considered that mass inoculation of whole populations should be undertaken except under very special circumstances.

ii. The first part of this paper is concerned with the routine methods employed by the author for the diagnosis of typhoid fever by the isolation of *Salmonella typhi* from blood, faeces and urine cultures. The methods used are generally those employed by all clinical bacteriologists and call for no comment. It is, however, surprising that no mention is made of culture from blood-clot which most bacteriologists favour at the present time. The author is presumably well satisfied with the results he obtains from whole blood cultures in bile-broth.

Serological reactions are not much employed for diagnosis, and the Vi-agglutination test as a screening procedure for the detection of typhoid carriers, although it appears to be recommended by the Health Authorities in South Africa, is not favoured by the author. In his opinion the only reliable method for the detection of carriers is an intensive epidemiological investigation followed by a series of full bacteriological examinations of the faeces and urine of all suspects.

iii. This article is of the same nature as that by TURNER (above). It does not contain any information with which bacteriologists are not already familiar and although it pays more attention to the biochemical reactions of the intestinal Gram-negative bacilli it follows the same general lines as the previous article with regard to the routine diagnosis of typhoid fever.

iv. The author deals with this subject as an administrative medical officer of health. The commonly accepted methods of spread of typhoid fever and the standard methods of prevention, including public and personal hygiene, are briefly considered. In dealing with the carrier problem he follows the lines set out by TURNER (above). He strongly recommends the registration of all known typhoid carriers together with their phage-type. In South Africa the phage typing of all strains of newly isolated typhoid bacilli is undertaken in Professor Pijper's laboratory in the Institute of Pathology, Pretoria. *H. J. Bensted*

LOCKETT, H. I. **Human *Salmonella typhimurium* Infection acquired from Poultry.** *Med. Officer.* 1959, Aug. 28, v. 102, No. 9, 87.

This is a report of a successful epidemiological and bacteriological investigation of an isolated incident of acute gastro-enteritis which eventually proved to be due to an infection acquired from locally kept poultry. A family consisting of father, mother and 6 children had recently taken delivery of a small consignment of one-day-old chicks. The chicks sickened and gradually died off except for one which appeared to be healthy.

During this period the mother fell ill with an acute gastro-enteritis. The possible connexion between the sickness of the chicks and the illness of the mother was considered and full bacteriological tests of the whole of the family and of the remaining chick, which had just been killed, were immediately undertaken. The gastro-enteritis in the mother was found to be due to a *Salmonella typhi-murium* and the same organism was isolated from the stools of 3 of the children and also from the spleen, liver and intestines of the chick. All the strains isolated proved to belong to phage type 2c. The evidence is therefore fairly conclusive that the chicks were already infected with *Salm. typhi-murium* at the time of delivery to the family, the members of which presumably contracted their infections either directly or indirectly from the infected birds.

H. J. Bensted

BLACK, V. H. A., CLARK, D. H. & TYSER, P. A. **A Hospital Outbreak of Flexner Dysentery including the Discovery of a Case of** *Shigella sonnei*. *Med. Officer*. 1959, Aug. 14, v. 102, No. 7, 61–3.

This discription of an outbreak of Flexner dysentery in a mental hospital would have been of greater interest had the responsible organism not been *Shigella flexneri* 3. Ever since specific type identification of the Flexner organisms has been possible there have been few outbreaks of bacillary dysentery in mental hospitals that have not been due to Type 3. In the particular hospital in which the outbreak described here occurred there are records of several "incidents" over the last 10 years in which Flexner organisms have been isolated from the patients; in all but one of these the organism was identified as *Sh. flexneri* 3. The peculiar endemicity of Flexner dysentery in mental institutions is well recognized and the irregular intermittent excretion of the organism during convalescence greatly increases the difficulty of organizing a workable, and at the same time reliable, system of clearance tests. After a long series of negative examinations, it is no uncommon experience to find a single stool containing *Sh. flexneri*. 1 example of this occurred in the outbreak described here among the 30 individuals involved. Why the single excretor of *Sh. sonnei* did not infect other members of the community is difficult to explain.

H. J. Bensted

PRIMACHENKO, M. B. **The Intradermal Reaction in Dysentery.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 12, 1888–94, 3 figs. [13 refs.] [Translated from Russian.]

Using Boivin type antigens, comprising the specific O-antigens and the bacterial endotoxins, of *Shigella flexneri* and *Sh. sonnei*, the author skin-tested some 470 persons suffering from acute and chronic bacillary dysentery, typhoid and gastro-enteritis, together with normal controls. Erythema at the site of inoculation extending over an area of more than 1 cm. diameter with induration was regarded as a positive reaction; erythema of less intensity was recorded as negative. In general it was found that normal controls, those suffering from intestinal conditions other than dysentery and those during the first few days of an acute attack of bacillary dysentery gave positive intradermal reactions. With the development of immunity, from the end of the first 10 days onward, the sensitivity to the antigen tended to fade. In those who did not respond to treatment or who relapsed the positive reaction continued. Moreover, so long as the stools contained blood and mucus the skin reaction tended to remain positive and the test was therefore of prognostic value for it confirmed that while the pathological stool continued, immune reactions were delayed. The specificity of these intradermal tests was demonstrated by the use of separate Flexner and Sonne antigens in cases where the causative organism was isolated and identified by full bacteriological procedures. *H. J. Bensted*

DARRICARRERE T., R., BULL B., F. & STANGE, Ruby. Frecuencia de aislamiento de *Escherichia coli* en la diarrea aguda del lactante en Concepción. [**Incidence of** *E. coli* **in Infant Diarrhoea in Concepcion, Chile.**] *An. Med. Concepción*. 1958, June, v. 15, Nos. 1/2, 15–19. [16 refs.]

The authors examined the stools of 340 infants under 2 years of age admitted to hospital with diarrhoea, and 89 healthy infants. *E. coli* type O111 was isolated from 18·8% and type O55 from 15·9% of the sick, and both types from 7·6%. Type O111 was associated with salmonella or shigella in 7 subjects, and O55 in 3.

In the healthy infants the incidence was much lower, 2·2% for type O111 and 3·4% for type O55.

The strains were susceptible to tetracycline and chloramphenicol. *Charles Wilcocks*

UTTLEY, K. H. **The Epidemiology of Tetanus in the Negro Race over the last Hundred Years in Antigua, the West Indies.** *West Indian Med. J.* 1959, Mar., v. 8, No. 1, 41–9.

Antigua is one of the Leeward Islands; its very limited area of 108 square miles carries a population which has risen from 36,000 in 1861 to 55,000 at the present day. Registration of all the births and deaths was made compulsory in this Colony in 1856, and from these registers the author has abstracted details of all Negroes and coloured persons certified as having died of tetanus, trismus or lockjaw.

Tetanus in Antigua, as in many backward tropical countries, occurs in 2 clearly defined forms, tetanus neonatorum and tetanus following trauma in later life. 2,134 examples of the disease, occurring during the past 100 years, have been analysed.

Tetanus neonatorum, defined as an infection occurring in the first 21 days of life, was equally prevalent in rural and urban areas. It provided a grave menace to infant life during the first 60 years of the period under review, causing from 8 to 33% of all neonatal deaths. Even the institution of a well organized midwifery service in 1880 failed to diminish its stature until a general advance in the knowledge and practice of hygiene took place during the first 2 decades of the present century, when its incidence rapidly declined to extinction in 1957, in which year 1,744 infants were born.

In later life, post-traumatic tetanus has shown a mortality 3 times higher in males than in females, with the highest incidence in the second quarter of the year, and the next highest in the first quarter. These periods, in this order of precedence, are the driest and most dusty, and are the season of sugar-cane harvesting when agricultural labourers, who form the bulk of the coloured population, are most exposed to cuts and abrasions. The highest death rate from traumatic tetanus was found in the decade 1887–1896, when it amounted to 21 per 100,000, but it remained between this figure and 13 per 100,000 until 1917–1926, since when it has ranged from 6 to 9 per 100,000. In 1957 the figure was notably less, namely 2 per 100,000. Corresponding figures in Great Britain have been stated as 5 per million in 1930 and 2·5 per million in 1948 [this *Bulletin*, 1951, v. 26, 892].

[No explanation is offered for the decline in the incidence of post-traumatic tetanus in recent years, despite the absence of mass immunization.]

J. H. Walters

VAKIL, B. J., TULPULE, T. H. & VERKEY, C. C. **Chlorpromazine in the Management of Tetanus. A Report of 340 cases.** *J. Ass. Physicians India.* 1959, July, v. 7, No. 4, 303–9. [20 refs.]

Of 340 patients treated between 1956 and 1958, 259 failed to respond to routine sedation with chloral hydrate, bromides and quinalbarbitone sodium (seconal): they were therefore given chlorpromazine in addition. The drug was given mainly by intravenous drip, 50–100 mgm. every 6 hours being a common dose: a total of 1 gm. per day was rarely exceeded. The authors found the effect gratifying, spasm and rigidity being much reduced. Of the 340 patients, 88 died; this compared with an earlier group of 361 patients who had no chlorpromazine and of whom 124 died. The authors regard chlorpromazine as a useful adjuvant in the treatment of tetanus. *A. B. Christie*

NAZARETH, F. A. & EDIBAM, B. C. **Chlorpromazine in the Management of Tetanus Neonatorum.** *Indian J. Child Health.* 1959, July, v. 8, No. 7, 349–56. [18 refs.]

The mortality of tetanus neonatorum was so high in Bombay that hospital authorities were unwilling to admit cases of a disease where "the mortality is about a hundred per cent.". Of 16 patients treated by the authors with chlorpromazine, 7 recovered, a mortality rate of 56·2%. The drug was given intramuscularly in a daily dose up to 6½ mgm. per lb. body weight given in divided doses every 6 or 8 hours. Anti-tetanic serum, quinalbarbitone sodium and penicillin were given as well. No toxic effects from chlorpromazine occurred. The authors are not entirely satisfied with chlorpromazine in tetanus neonatorum and think their dosage may not yet be high enough but they regard the use of the drug as a definite advance in the treatment of this highly fatal disease. *A. B. Christie*

HUNTER, W. F. **Tetanus Prophylaxis.** [Correspondence.] *Med. J. Australia.* 1959, July 18, v. 2, No. 3, 98–9, 1 fig.

This letter is a well-reasoned attack on the prophylactic use of antitetanic serum. There is no way of knowing which wound is liable to produce tetanus—in many cases the wound is quite trivial. Repeated injections of antitoxin lead to a state in the body when antitoxin is so rapidly excreted as to be useless as a prophylactic. There are many complications of antitoxin prophylaxis, some of them serious or fatal. Tetanus not infrequently occurs even after the use of tetanus antitoxin—in fact it is difficult to prove that tetanus antitoxin does prevent tetanus. There is always a medico-legal difficulty in not giving tetanus antitoxin but the author suggests that a doctor might instead be sued for giving antitoxin and exposing his patient to the dangers of a therapy of doubtful value. The only sound preventive is active immunization.

[This long letter is worth careful study.]

A. B. Christie

SOLOSHENKO, I. Z. **The Part played by Blood-Sucking Arthropoda in the Transmission and Harbouring of Pathogenic Leptospires—I. The Part played by Blood-Sucking Arthropoda in the Transmission and Harbouring of the Organism of Weil's Disease.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 1/2, 19–23. [12 refs.] [Translated from Russian.]

Serological evidence of infection with *Leptospira icterohaemorrhagiae* was found in 10/150 grey rats [*Rattus norvegicus*] caught in the province of Abkhazia [situated in Caucasia] and strains of *L. icterohaemorrhagiae* were isolated from 5 of these rats. Among other rodents examined, agglutinins for *L. pomona* were found in sera from 1/13 black rats [*R. rattus*], 1/23 house mice [*Mus. musculus*] and 2/8 field mice [? *Apodemus* sp.]. Antibodies for *L. grippotyphosa* were present in 1/4 wood mice [probably *A. sylvaticus*], but no strains of leptospires were isolated from any of these rodents.

The ectoparasites of the *R. norvegicus* were collected and identified, and guineapigs were inoculated [with apparently pooled material] to determine whether any of the ectoparasites were carriers of leptospires. No infections resulted. Attempts were made to transmit *L. icterohaemorrhagiae* by feeding mites, ticks, lice or fleas on infected guineapigs but successful results were obtained only with *Ornithonyssus bacoti*, up to 25 days after the infective feed, and with *Hyalomma asiaticum*, up to 30 days [but *H. asiaticum* is not shown in the list of ectoparasites found on grey rats]. *J. C. Broom*

FRAGA DE AZEVEDO, J. & FARO, M. M. da C. Sur la presence de la *Leptospira hyos* au Portugal. [**Presence of *Leptospira hyos* in Portugal**] *Anais Inst. Med. Trop.* Lisbon. 1958, Dec., v. 15, No. 4, 855–66, 2 figs. [29 refs.]

The English summary appended to the paper is as follows:—

"The research of leptospira in the kidneys of 94 pigs

from several parts of Portugal, slaughtered in the Lisbon Municipal Slaughterhouse, permitted us to isolate 17 strains of which it was possible to keep 15 in the laboratory.

"From the isolated strains 7 were identified as *Leptospira pomona*.

"The serological characterization of the 15 strains made later, showed that 9 should be identified as *L. pomona* and 6 as *L. hyos*, a serotype that is thus referred for the first time in the country, where it seems to be largely distributed."

VIRUS INFECTIONS

The order in this section is:—*General, Psittacosis-Lympho-granuloma group, Pox group, Respiratory group, Enteric group, Arthropod-borne group, Others.*

BRAUNER, R., LACK, H., BUCUR, N., SĂRĂTEANU, D. & DRĂGANESCU, N. Considerații asupra unor cazuri de ornitoză. [**Remarks on Cases of Ornithosis**] *Studii si Cercetări Inframicrobiol.* 1959, v. 10, No. 1, 31–8. French summary.

The following is a translation of the French summary.

81 cases of pulmonary disease were examined by means of the complement-fixation test with an ornithosis antigen; the clinical picture was in general atypical.

8 of the subjects were identified as cases of ornithosis because they gave positive complement fixation in rising titre with successive specimens of serum.

25 who gave positive reactions on one occasion, and could not be tested again, were regarded as suspected cases.

Clinically the onset was generally brusque, with pain in the chest, chill and high temperature, and more rarely insidious, with symptoms resembling influenza. Functional effects included a dry cough with scanty sputum, sometimes dyspnoea, cyanosis and a deterioration in the general condition with marked asthenia. Signs detectable with the stethescope were slight in comparison with the symptoms and radiological signs. The fever lasted 7–14 days, but protracted illness, lasting even more than a month, was also observed. Radiologically, hilar forms, parenchymatous forms in which the pulmonary infiltration was continuous to the hilum, and bipolar forms, have been observed.

These are the first cases of ornithosis reported from Rumania. *Charles Wilcocks*

i. PANDIT, C. G., MASILAMANI, S. E. D., KRISHNAN, G. N. V. & SEAL, S. C. **Smallpox in Madras City—a Study in Retrospect.** *Indian J. Pub. Health.* 1959, July, v. 3, No. 3, 245–60, 1 fig.

ii. MATHEN, K. K. **Statistical Assessment of the Efficacy of Vaccination from the Data of the Child Population in the City of Madras during the Period 1945–50.** *Indian J. Pub. Health.* 1959, July, v. 3, No. 3, 261–7, 1 diagram.

i. "An exhaustive statistical study of properly maintained records of smallpox in Madras City in the recent years, has provided strong and incontrovertible evidence in favour of vaccination and revaccination. The attack rates as well as death rates were several times higher among the unvaccinated than in the vaccinated groups.

"Judged by the severity of rashes and the mortality rates it would appear that revaccination offered better protection over primary vaccination. Revaccination 'takes' (i.e., those with evidence of reaction) proved superior to revaccination 'failures' and the latter in turn proved superior to the primary vaccinated group. Another interesting finding was that vaccination done even during the incubation period was better than no vaccination at all.

"The extent of scar area would seem to give an approximate measure of the degree of immunity conferred. For example, persons with 4 scar marks always fared better as judged by the incidence of the disease, the severity of lesions and the mortality rates."

ii. "In this paper an attempt is made to estimate the efficacy of vaccination in protecting against smallpox attack. The paper is meant as a complement to the paper above and a more detailed analysis of available data is done in this paper, in order to ensure that the assumption that some of the factors considered insignificant does not really affect the conclusions arrived at in the basic paper. The factors considered for evaluating their effect on the main conclusion are (1) since vaccinations are performed throughout a calendar year the children vaccinated are in the vaccination status only for part of the year, (2) the population in any age-group observed in one year are not all in that age-group throughout the year because some of them when they complete that age period cease to be in the group observed, (3) deaths take place all through the year and those who die in the calendar year of observation are under observation for varying periods and (4) those who leave and enter the area under study during the period of observation, do so at varying times during the period. The effect of the above factors on the comparison between the smallpox attack rates of the vaccinated and the unvaccinated groups has been estimated, under certain general assumptions. After making the above correction, it has been found that the difference between the smallpox attack rates of the two groups are still highly significant, thereby confirming the conclusions arrived at in the earlier paper referred to."

[This is an exhaustive and painstaking study. But, for example, because the statistics and other data on which it is based were not compiled on a design planned for the purposes of this investigation, some loss of accuracy must be accepted. Again, among other things, one must have doubts about the recorded deaths accredited to smallpox in infants under 1 year "vaccinated with marks visible" and wonder what part smallpox did play in the fatal issue of such cases.

The authors speak as though theirs were the first study of its kind aimed at evaluating the effect of vaccination and re-vaccination in the prevention or amelioration of smallpox. In fact, their conclusions—including those regarding the relationship of scar area to protection—have for long been accepted in the United Kingdom, largely from experience gained in the 1900–02, 1926–34 and previous epidemics.] *J. Pickford Marsden*

HERRLICH, A., MAYR, A. & MAHNEL, H. Das Antikörperbild der Variola-Vaccineinfektion. 2. Mitteilung. Serologische Untersuchungen an Variolapatienten. [**The Antibody Production of Infections with Variola and Vaccinia Virus. 2nd Communication: Serological Investigations of Variola Patients**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 3/4, 163–82, 9 figs.

The authors investigated antibody levels in 164 smallpox and 9 alastrim patients. They measured antihaemagglutinin, precipitin and complement-fixing antibodies. In complement fixation they tested for antivirus antibodies (V) and for anti-soluble antigen antibodies (S). Precipitins were tested by an agar diffusion method. The disease in the smallpox patients was of varying degrees of severity from discrete smallpox through confluent to haemorrhagic.

In discrete, confluent and secondary haemorrhagic cases, the titres of haemagglutinin inhibiting, precipitating and complement-fixing V antibodies reached a peak, usually after the 10th day of illness. S antibodies were generally absent or of low titre. Most of the patients with primary haemorrhagic disease were dead by the 10th day. Antibody titres in these cases tended to be low, and antihaemagglutinin was more likely to be present than the other types of antibody. In 9 cases of alastrim, antihaemagglutinin was absent even at the 18th day of illness; complement-fixing V antibodies were present in 3 cases only, at low titres. In 29 cases of modified disease in previously vaccinated people antihaemagglutinin behaved much the same as in the milder cases of variola major. Precipitating and complement-fixing V antibodies seem to have responded rather more briskly.

The agar gel diffusion method for precipitating antibodies was the simplest test to apply, but inhibition of haemagglutination gave more positives than any of the methods used. *Colin Kaplan*

GABLE, J. J., Jr. **Primary Chickenpox (Varicella) Pneumonia: Report of Two Cases seen in the Private Practice of Internal Medicine.** *Ann. Intern. Med.* 1959, Sept., v. 51, No. 3, 583–90, 2 figs. [16 refs.]

Cases of primary chickenpox pneumonia have been reported with increasing frequency in recent years in contrast to the paucity of previous experience of this condition [this *Bulletin*, 1957, v. 32, 228, 642; 1958, v. 33, 552]. This rise does not appear to be associated with any increased virulence of the virus, although most cases of varicella pneumonia have been seen in adults, among whom the disease naturally tends to be more severe than in children.

Case reports are given here of 2 young women who contracted chickenpox from their children and each of whom, a few days after the appearance of the eruption, became acutely ill, cyanotic and dyspnoeic; with scattered adventitious sounds in the chest, pleural pain and viscid blood-stained sputum. X-ray examination of the chest revealed diffuse infiltration involving all lobes of both lungs. Treatment was symptomatic: steroid therapy was considered to be contra-indicated: high concentrations of oxygen were needed. Once the acute stage was over convalescence was rapid: but complete clearing at the lung bases may be delayed for several months. *J. Pickford Marsden*

POLAK, M. F. Influenzasterfte in de herfst van 1957. [**Influenza Mortality in the Autumn of 1957**] *Nederl. Tijdschr. v. Geneesk.* 1959, May 23, v. 103, No. 21, 1098–109, 4 figs. English summary.

During the epidemic of Asian influenza in the Netherlands in 1957, 337, 782 and 111 fatal cases occurred in September, October and November, representing an average mortality over the period of 11·2 per 100,000 population. The mortality was least in the 20–29-year age-group (3·0 per 100,000), and rose in older age-groups to attain 171·2 per 100,000 (232 cases) in persons aged 80 years and over. Below 40 years of age the mortality was somewhat higher in females; it showed great variations between different provinces (from 23 to 1,230 per 100,000), and was greater in small communities (14·5 per 100,000 in places with less than 5,000 inhabitants) than in large towns (7·7 per 100,000 in populations exceeding 100,000). The peak in the average mortality was attained in the second week of October (273 cases), and data are quoted for the peak incidence in different parts of the country for different age and population groups, and also for the effect of pre-existing diseases upon the mortality from influenza. *D. J. Bauer*

BRUYN, H. B. & LENNETTE, E. H., with the technical assistance of Florence W. JENSEN & Lorraine TAUBER. **Immunological Evaluation of Monovalent Influenza Vaccine in Adults and in Children.** *Arch. Intern. Med.* 1959, June, v. 103, No. 6, 914–23. [22 refs.]

Antibody response to a monovalent Asian influenza vaccine was studied among 133 children under 15 years of age and 142 adults over 50 years old. Complement-fixing antibody to influenza A was found in pre-vaccination sera of 11% of the children aged 1–5 years, 28% of children aged 6–15 years, 82% of adults aged 50–70 years and 58% of the age-group of over 70 years. Asian influenza haemagglutination-inhibiting antibody in pre-vaccination sera was not detected in any of the children but was found in 22% of adults distributed throughout the different age-groups. Good antibody responses were observed in adults given a single intradermal vaccine dose. This response was not significantly increased after a second intradermal injection and was comparable to that following the subcutaneous administration of larger vaccine doses. No significant antibody response could be demonstrated in children given a single intradermal dose of vaccine. Antibody rises comparable to those obtained in adults were however observed in children given a second injection. The level of antibody response was independent of volume (0·1 or 0·2 ml.) or antigen concentration (20, 40 or 80 chicken cell agglutinating units) administered by the intradermal route. *H. G. Pereira*

PROWSE, C. B. & COLLINS, D. M. **The Prognosis in Post-Influenzal (Asian) Pneumonia.** *Brit. J. Clin. Practice.* 1959, Aug., v. 13, No. 8, 554–60, 7 figs.

35 patients suffering from post-influenzal pneumonia were studied in the Brighton area by the author during October 1957: the average age was 52 years, the range being 15 to 74 years. 14 of the 35 patients died. The 2 indications of a bad prognosis were associated or complicating non-respiratory diseases and radiological evidence of bilateral pulmonary involvement. On the other hand, previous respiratory disease did not necessarily indicate a bad prognosis. *A. B. Christie*

GRAYSTON, J. T., WOOLRIDGE, R. L., LOOSLI, C. G., GUNDELFINGER, B. F., JOHNSTON, P. B. & PIERCE, W. E. **Adenovirus Infections in Naval Recruits.** *J. Infect. Dis.* 1959, Jan.–Feb., v. 104, No. 1, 61–70, 1 fig. [17 refs.]

In this systematic study of random samples of U.S. naval recruits in a training centre for evidence of adenovirus infection over a period of 1 year, 28 adenoviruses were isolated from 647 samples (4·4%) and 188 positive complement-fixation tests were demonstrated in 1,155 paired sera (16%); 7 of the 28 men whose swabs were positive for adenovirus had no symptoms of respiratory disease. In the first 6 weeks of training, while the adenovirus isolations occurred in 4% of the recruit population 59% of those swabbed had some respiratory symptom or symptoms, most of which could not, however, on the virological and serological findings be attributed to adenovirus infection. Type 4 adenovirus was the main type isolated and determined serologically.

It is concluded that mild illnesses due to adenovirus infection as well as asymptomatic infections with these viruses have been demonstrated, but that illness due to adenovirus infection alone, or in combination with other agents, may exhibit a wide range of severity. [See also this *Bulletin,* 1957, v. 32, 230.] *H. Stanley Banks*

COOK, G. T. **Isolation of Poliovirus and Coxsackie B Virus in West Surrey, 1958.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Aug., v. 18, 138–43.

The value of tissue culture methods for the routine diagnosis of poliomyelitis and illnesses suspected of being poliomyelitis is illustrated. The results of the examination of 698 specimens (faeces or throat swabs) for viruses in HeLa cells are presented. In all, 32 polioviruses (all type 1) and 53 Coxsackie B viruses (B3 or B4) were isolated. Poliovirus was isolated from 5 of 8 patients with paralytic poliomyelitis (from both of 2 children) and from 9 of 57 with non-paralytic illnesses (these yielded 12 Coxsackie B viruses). Poliovirus was isolated from 60% of household contacts of paralytic and only 7·5% of contacts of non-paralytic cases. Coxsackie B virus was isolated from 18% of children with upper respiratory infection. This virus was also isolated from 3% of healthy children aged 0–4 during a survey of faeces for poliovirus during the year (no polioviruses were isolated). There was no seasonal incidence for polioviruses but the great majority of the Coxsackie B were isolated during April to August. Coxsackie B3 and B4 were isolated from persons in distinctly different communities. *A. J. Beale*

SIGGIA, S. & PINTO, V. Aspetti epidemiologici della poliomielite in Italia. **[Epidemiological Aspects of Poliomyelitis in Italy]** *Ann. d. San. Pubblica.* Rome. 1959, May–June, v. 20, No. 3, 455–513, 8 graphs. [87 refs.] English summary.

The authors refer to BODIAN'S theory of the pathogenesis of poliomyelitis infection [this *Bulletin,* 1956, v. 31, 496] which assumes a clinically silent intestinal phase, a viraemic lymphatic phase giving rise to abortive forms, and a nervous phase which gives rise to both paralytic and non-paralytic forms. The finding of neutralizing antibodies may indicate either recent or remote infection, while the deviation of complement is suggestive of recent infection. Extensive epidemics in Italy have generally been found to be due to Type 1, while Type 3 has been isolated in the second wave of limited epidemics; Type 2 has not been found associated with epidemics or even with circumscribed foci of the paralytic form. At all ages, exposure to the virus gives rise to the production of antibodies, whether there are clinical manifestations or the infection remains latent.

The disease has been notifiable in Italy since 1923 and this paper includes tables and graphs of yearly records and regional distribution going back to 1936, and in some cases even to 1924. Except for a flare-up in 1939 (13·7 per 100,000) and discounting the wartime abnormal period of 1942–45, the incidence has shown no substantial fluctuations between 1936 and 1955 but it has been rising since 1956—apparently owing to locally limited outbreaks rather than to a nation-wide increase. In the islands and the southern parts of the mainland, the year-to-year incidence is more suggestive of endemicity.

From a low level in the first 3 months of the year, there is a gradual rise towards a summer peak, sometimes with a smaller second wave in the autumn. 85% of the cases affect the 0–4 age-group, but the age at which infection takes place tends to be higher in the town than in the country. Males are affected more frequently than females. Italian workers have confirmed the role of fatigue and trauma as predisposing factors in the aetiology of the paralytic forms of poliomyelitis, but they have failed to demonstrate any association with prophylactic inoculations. Nevertheless, they advise that immunization should be undertaken in the winter months, preferably during the second half-year of life, and that prophylactic injections and surgical operations should be avoided as far as possible during an epidemic.

The authors discuss how latent and subclinical infections give rise to the development of immunity and how this is affected by varying standards of living as observed among under-developed and advanced communities respectively. *J. Cauchi*

GASPARINI, V., MAJORI, L. & FARISANO, G. Isolamento di virus poliomielitici nella popolazione infantile del Veneto, negli anni 1957–1958. [**Poliomyelitis Viruses isolated in Children in Veneto during the Years 1957–58**] *Ann. d. San. Pubblica.* Rome. 1959, May–June, v. 20, No. 3, 527–30. English summary (5 lines).

These authors have studied the distribution of poliomyelitis virus among 251 children aged 10 months to 10 years in the provinces of Venice, Padua, Verona, Udine and Trento between epidemic periods: 88 of the subjects were inmates of children's homes and the other 163 belonged to private households. Employing tissue culture techniques which they outline, they isolated 47 strains (18·72%) from the 251 stool specimens. This rate is somewhat higher than those found in other parts of Italy, which ranged from 0·5 to 13·4% varying with the locality.

Of the strains from the present survey, 39 were Type 1, 7 Type 2 and 1 Type 3. A similar predominance of Type 1 has been found in the distribution of immunity and the incidence of the paralytic form of the disease among the population of these parts of Italy.

J. Cauchi

MAJORI, L., GASPARINI, V. & GAMBA, F. Iso'amento di virus poliomielitici negli anni 1957–1958 da casi clinici di polioparalisi, nel Veneto. [**Poliomyelitis Viruses isolated in Paralytic Poliomyelitis Cases occurring in Veneto during the Years 1957–58**] *Ann. d. San. Pubblica.* Rome. 1959, May–June, v. 20, No. 3, 531–6. [20 refs.] English summary (2 lines).

The authors of this paper have studied the distribution of the 3 types of poliovirus among paralytic cases of the disease in the provinces of Padua, Trento, Udine and Verona and they describe the tissue culture techniques which they have employed in this investigation.

Specimens of stools were taken from 144 patients and from these they isolated 94 strains (65·28%), 82 being Type 1, 11 Type 2 and the remaining strain Type 3. They give details of their findings in each of the 4 provinces and conclude that their results differ little from previous findings by other Italian workers in the rest of the country. *J. Cauchi*

GIORN. DI MALATTIE INFETTIVE E PARASSIT. 1958, Dec., v. 10, No. 12, 1261–331, numerous figs. [Numerous refs.] Società Italiana per lo Studio delle Malattie Infettive e Parassit. Convegno Nazionale sulla Poliomielite con la collaborazione della Società di Cultura Medica Novarese (Novara, 27 ottobre 1957). **[Italian Society for the Study of Infective and Parasitic Diseases. National Conference on Poliomyelitis, Novara, October, 1957.]**

The first subject for discussion was modern treatment in the acute stage of poliomyelitis. Various medicaments have been used, including antibiotics and vitamins, with transfusion of blood or plasma, radiotherapy or other procedures. But much of this section is devoted to physical methods. Results obtained in considerable numbers of patients are given by various authors. The second subject was treatment after the acute stage, and here the physical methods are prominent, but attention is also paid to psychotherapy. The third subject deals with the work of convalescent homes and the timing of treatment and the need for continuity.

The whole symposium should be useful to those who wish to know current Italian practice.

Charles Wilcocks

GIORN, DI MALATTIE INFETTIVE E PARASSIT. 1958, Dec., v. 10, No. 12, 1333–447, numerous figs. [Numerous refs.] Società Italiana per lo Studio delle Malattie Infettive e Parassitarie. Convegno Piemontese sulla poliomielite (Torino, 15 Giugno 1958). **[Italian Society for the Study of Infective and Parasitic Diseases. Conference on Poliomyelitis, Turin, June, 1958.]**

This publication is in effect a monograph on the new aspects of poliomyelitis. DE MATTIA and 7 colleagues have collaborated, and the monograph is in 4 chapters dealing respectively with the acute phase of the disease, the cultivation of the virus in tissue culture as a means of diagnosis, the distribution of antibodies in the population of Turin and district, and the lesions of the central nervous system which are outside the motor pathways.

There are many illustrations, some of the tissue culture cells, and more of the central nervous system lesions. *Charles Wilcocks*

PERKINS, F. T., YETTS, Risha & GAISFORD, W. **Responses of 6- and 9-months-old Infants to Two and Three Doses of Poliomyelitis Vaccine.** *Brit. Med. J.* 1959, Sept. 26, 530–32, 1 chart.

The authors have previously investigated the response of very young children to poliovaccine. They found that the immunization of very young infants was unsatisfactory mainly because of high levels of maternally transmitted antibody [PERKINS *et al.*, this *Bulletin*, 1958, v. 33, 1021; 1959, v. 34, 735, 736]. They now report an investigation of the response of infants aged 6 months and 9 months to 2 and 3 doses of vaccine, each dose being of 1 ml. spaced at intervals of 4 weeks. Blood samples were obtained 4 weeks after the second dose and 14 to 21 days after the third dose. None of the infants aged 9 months and only 2 of those aged 6 months had inhibitory levels, that is 1/64 or greater, of maternally transmitted antibody at the time of commencement of the vaccination course.

2 vaccines were used in this investigation, the first contained the Bruenders strain for the type 1 component as employed by manufacturers in Britain and the other vaccine had the Mahoney type 1 component. The response of all the infants to 3 doses of vaccine was excellent for all 3 types of vaccine. The benefit of the third dose was reflected in much higher titres for types 2 and 3 and for type 1 not only in a higher geometric mean titre but also in a higher proportion of the infants responding. Indeed, for type 1 the proportion of children responding was unsatisfactory with 2 doses. The geometric mean titres after 2 and 3 doses respectively for the 3 types of virus were as follows: for the 6-month infants type 1, 1/39 and 1/870, for type 2, 1/140 and

1/1080 and for type 3, 1/122 and 1/1140; for the 9-month children for type 1, 1/8 and 1/71, for type 2, 1/100 and 1/1378 and for type 3, 1/134 and 1/1520. The differences in response of the 6-month and 9-month children suggest that the potency of the type 1 component used for the younger children was much superior. This difference was only partially reflected by the results of the monkey potency tests on the 2 vaccines.

It is concluded from these results that it is satisfactory to vaccinate infants aged 6 months provided 3 doses of vaccine are used for the primary course. *A. J. Beale*

Oddo, F. G., Flaccomio, R., Priolo, A. & Santamaura, S. Risposta anticorpale a vaccino antipoliomielitico (tipo Salk) in un gruppo di bambini nel primo quadriennio di vita. [**Antibody Response to a Salk-type Poliomyelitis Vaccine in a Group of Children under 4**] *Riv. Istituto Sieroterap. Ital.* 1959, May–June, v. 34, No. 3, 225–35, 5 graphs. [10 refs.] English summary.

This study was carried out on 21 children ranging in age from 4 months to 3½ years in a district near Palermo. The vaccine prepared by the Istituto Sieroterapico Italiano contained Brunhilde, MEF-1, and Saukett strains. It was given in 1 ml. doses with intervals of 10 weeks between the first 2 doses and of about 5 months between the second and third. 5 serum samples were examined.

The most complete and most persistent response was that against MEF-1. After the third inoculation, in children who had some before treatment, there was a moderate rise in antibodies against Brunhilde and Saukett and a more marked rise against MEF-1. Among those who had no antibodies initially, 9 out of 13 developed antibodies against Brunhilde, 16 out of 16 against MEF-1, and 13 out of 15 against Saukett. Apparently on the basis of the nature of the antibody curve, it was deduced that there was an intercurrent infection with poliomyelitis during the course of vaccination in 10 cases and the rises in antibodies attributable to these (shown in the graphs by white rings) are distinguished from those due to the vaccines.

E. Agius

Cox, H. R., Cabasso, V. J., Markham, F. S., Moses, M. J., Moyer, A. W., Roca-Garcia, M. & Ruegsegger, J. M. **Immunological Response to Trivalent Oral Poliomyelitis Vaccine.** *Brit. Med. J.* 1959, Oct. 3, 591–7, 2 figs. [12 refs.]

Up to the present one of the drawbacks of attenuated poliovaccine has been the necessity for administering the 3 types of poliovirus separately in order to overcome interference between the types [this *Bulletin*, 1956, v. 31, 801; 1957, v. 32, 1032]. This paper presents results suggesting that this objection has been largely overcome. With the strains developed by Lederle Laboratories (SM type 1, MEF 1 type 2, and Fox type 3) each in a dose of $10^{6.1}$ TCD50 contained in 2 ml., it was found that the antibody response to a single dose in 188 volunteers was extremely good. The volunteers and members of their families ranged in age from 4 years to 60 but the majority were aged from 21 to 50 years. There were 11 triple negatives, 18 who were negative to types 1 and 2, 7 negative to types 2 and 3, and 10 negative to types 1 and 3. In addition there were 14 negative to type 1 only, 6 to type 2 and 30 to type 3 poliovirus before the administration of vaccine.

The antibody responses showed that 51 out of 53 persons who lacked type 1 antibodies developed them after vaccination and all of the 58 negatives to type 3 virus also developed antibodies whereas only 33 out of 42 negative to type 2 showed an antibody response. The antibody responses of persons with prior antibodies were more variable and, indeed, became less frequent the higher the pre-feeding antibody titre. Thus with titres of 1/64 or more less than 50% of the individuals showed an antibody response to vaccination. The response to smaller doses of vaccine were less good. The authors note that these encouraging results were obtained in a preliminary study and suggest that better results might be obtainable if the vaccine were given at a special time of day, for example after a meal, and they also suggest that the second dose of trivalent vaccine might be given after 6 weeks to fill any gaps left by the primary vaccination. They also note that the results were obtained mainly with adults who are more difficult to infect than children. *A. J. Beale*

Smorodintsev, A. A., Davidenkova, E. F., Drobyshevskaya, A. I., Ilyenko, V. I., Gorev, N. E., Kurnosova, L. M. & Klyuchareva, T. E. **Results of a Study of the Reactogenic and Immunogenic Properties of Live Anti-Poliomyelitis Vaccine.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1053–74, 9 figs.

This paper contains a long-awaited account of Russian experience with Sabin's strains of attenuated poliovaccine. The paper reports studies carried out in Leningrad. The virus strains used were type 1 LSc, type 2 P 712-10 and type 3 Leon 14 ab. which were received in Leningrad in the early part of 1956. More attenuated variants of these strains have subsequently been obtained by Sabin, picking single plaques. In Leningrad the strains were given between 24 and 30 additional passages in monkey kidney monolayer cultures with massive doses of virus in the hope of producing more stable hereditary characters during the process of adaptation to extraneural tissue. Small batches of the vaccine were prepared and inoculated into rhesus monkeys intracerebrally and intraspinally and found to be similar in pathogenicity to the original strains according to Sabin's data.

The results of studying 22,201 children given 100,000 TCD50 and about 10,000 control contact children are described. They showed: (1) The vaccine was perfectly safe. (2) Virus was excreted from children who developed an antibody response. The duration of excretion varied but averaged about 35 days. Excretion was much lower in titre and of lesser duration when a second challenge dose of virus was given. (3) Contact infection was extremely prevalent for type 1, the great majority of contact children developing antibodies, but for types 2 and 3 less than half of the contact children developed an antibody response. (4) The virus excreted by vaccinated children and from contacts and in deliberate

experiments where virus isolated from one child was fed to other children through 8 human passages was often found to be of slightly higher pathogenicity for rhesus monkeys by the intraspinal route and occasionally also by the intracerebral route. There was no evidence, however, that with successive passages in human beings there was a uniform selection of the more virulent variants. (5) The immune response of vaccinated individuals was excellent especially for those children, about 70% of the pre-school children, who lacked antibodies to all 3 types of virus. The responses were still good when type 1 was given first, followed 1 month or more later by a mixture of types 2 and 3. The response of individuals with pre-vaccination titres of 1/64 or greater was less good. It is concluded from these studies that the Sabin strains of poliovaccine are suitable for study in larger scale epidemiological experiments.

A. J. Beale

TRIER, S. Meningitis fremkaldt av ECHO 9 virus. En epidemi med 30 tilfae'de i Ringkjöbing amt 1958. [**Meningitis Provoked by ECHO 9 Virus. An Epidemic with 30 Cases in the County of Ringkjöbing 1958**] *Ugeskr. f. Laeger.* 1959, Sept. 10, v. 121, No. 37, 1390–96. 2 figs. [44 refs.]

In the latter half of 1958 small epidemics of meningitis in the Danish County of Ringkjöbing led to the admission to hospital of 30 cases presenting certain curious features. Only 6 of the patients were over the age of 20, and as many as 6 were under 5. The oldest was 47, and there were 21 male to 9 female cases. After an initial bout of fever with drowsiness, headache and anorexia there would be a pause of 4 to 5 days when the patient felt much better, only to start a high fever with violent headache, nausea and vomiting. Definite cervical rigidity, diffuse redness of the fauces, and microadenitis colli were noted, and after an average of about a week the cerebral and meningeal symptoms passed off and all the patients recovered. On the assumption, early in the epidemic, that the meningitis might be of bacterial origin, various antibiotics were given without much effect. Samples of faeces and cerebrospinal fluid sent to the poliomyelitis department of the State Serum Institute yielded the ECHO 9 virus in 7 out of 9 faeces samples and in 11 out of 20 cerebrospinal samples. Both samples having yielded this virus in 3 cases, the total number of patients with this virus was 15. The cell content of the cerebrospinal fluid was considerably higher in these cases than is supposed to be usual with meningitis of virus origin, and in 12 cases more than 40% of the cells were polynuclear. The treatment under which all these patients recovered was rest in bed while they were febrile.

Claude Lillingston

MEDEARIS, D. N., Jr. & KRAMER, R. A. **Exanthem associated with ECHO Virus Type 18 Viremia.** *J. Pediatrics.* St. Louis. 1959, Sept., v. 55, No. 3, 367–73. [23 refs.]

The authors describe an illness associated with fever in a baby 3 weeks old; as the fever subsided an intense blotchy erythematous rash developed. An 18-month-old sibling suffered from a similar illness. ECHO virus type 18 was isolated from the blood and throat and rectal swabs, and a rise in antibody to ECHO type 18 occurred in convalescence. The ECHO 18 strain showed minor antigenic differences from the prototype strain. It is thought that the illness and rash were due to ECHO 18 although it is conceded that the rash could have been due to the drugs used (acetaminophen and oxytetracycline).

[ECHO type 18 has previously been associated with an outbreak of diarrhoea in an infants' home, EICHENWALD *et al.*, this *Bulletin*, 1958, v. 33, 734.]

A. J. Beale

FRANCIS, R. D. & CEBALLOS, R. **Viremia in ECHO Type 6 Virus Infection.** *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 479–81.

A 7-year-old child had an illness of abrupt onset associated with muscle weakness of the lower limbs, with fever and a rapidly downhill course without signs of meningeal involvement, going on to death after 7 days of illness. ECHO 6 virus was isolated in human amnion tissue culture from the blood taken on the third day. Faeces and throat swabs and cerebrospinal fluid were negative for virus both in human amnion cells and in suckling mice. At autopsy no virus was isolated from sigmoid colon or its contents, the ileum, the mesenteric lymph nodes, cervical and lumbar cord, medulla, pons and cerebral cortex. Sera were obtained from 6 household contacts 3 months after the patient's fatal illness. Only 1 of these contacts, aged 14 years, possessed neutralizing antibodies to ECHO 6 virus. [See also this *Bulletin*, 1958, v. 33, 212; 1959, v. 34, 29.]

A. J. Beale

BENDA, R. & ONDRÁCEK, J. Aseptické meningitidy vyvolané ECHO virem (Typ 9) v kraji Hradec Králové roku 1957. [**Abacterial Meningitis evoked by ECHO Virus (Type 9) in the Hradec Králové Region in 1957**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 5, 328–41. [65 refs.] English summary.

ARNOLD, J. H. & ENDERS, J. F. **Disease in Macacus Monkeys inoculated with ECHO Viruses.** *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 513–16, 1 fig. [11 refs.]

KIBRICK *et al.* (*Ann. New York Acad. Sci.*, 1957, v. 67, 311) have described the clinical manifestations of patients infected with ECHO viruses type 6 and type 16. These two types of virus (type 6 SHO strain, type 16 HAR strain) as human amnion tissue culture fluids were injected intrathecally and intraspinally into rhesus and cynomolgus monkeys. Both viruses caused definite but mild signs of muscular weakness. There were also signs of meningeal reaction with pleocytosis in the cerebrospinal fluid. The cell count varied from 64 to 598 cells per cmm. By contrast, animals infected with heated virus (65°C. for ½ hour) failed to show any clinical sign of infection or more than 20 cells per cmm. in the cerebrospinal fluid. The results suggest that these two ECHO virus types can be added to the list of enteroviruses causing paralysis or muscle weakness in monkeys or man.

A. J. Beale

PETRILLA, A., SOLT, K. & VEDRES, I. **Some Epidemiological Characteristics of Viral Hepatitis in Hungary.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 2, 135–45, 8 figs.

Infective hepatitis was made notifiable in Hungary in 1950. In the present report 87,000 cases of hepatitis notified in the period 1952–57 are analysed. There has been an increase of incidence from 7,251 cases (69 deaths) in 1952 to 19,615 (169 deaths) in 1956. This increase is in part at any rate to be ascribed to more accurate notification.

In 1957 the morbidity rate per 100,000 inhabitants was 210·9 in Budapest and 191·5 in country districts with a case mortality rate of 1·0% in the city and 0·6% in the country. The seasonal incidence which reaches its peak in about October is described in some detail with reference also to the differences between the city and country experience by month.

Details of the age distribution of hepatitis are given in tables and a figure. Children aged 3–10 years had a considerably higher morbidity rate than the younger and the older age groups. Some of the age specific morbidity rates per 100,000 in 1957 were 132·1 at age 0–2 years, 488 at 3–6 years, 559·7 at 7–10 years and then falling with increasing age to 93·7 at 50–59 years. It was also demonstrated that hepatitis is much more frequent in the medical profession than in any other group of the population—in 1956 the general adult morbidity rate was 141 per 100,000, 476 for physicians (including "chemists"), and 985 for "ungraduated medical staff".

M. E. Delafield

TRLIFAJOVÁ, J., RAMPAS, J., KREDBA, V. & SOUSEK, O. II. Naše zkušenosti s aldolázovým testem. [**Our Experience with the Aldolaze Test. II.**] *Časopis Lékařů Českých.* Prague. 1959, Sept. 18, v. 98, No. 38, 1195–201, 4 graphs. [34 refs.]

The English summary appended to the paper is as follows:—

"1. Using the aldolase test in the modification of Tovarnicki, a total of 919 persons, including 490 adults and 429 children were examined.

"2. There were 134 adults with a diagnosis of infectious hepatitis (IH) and 293 children with the same diagnosis. The serum aldolase level in IH depends on the stage of the disease and decreases gradually. In the majority of patients it is greatly increased during the first ten days in children and the first two weeks in adults.

"3. In two cases of IH in children greatly increased values of serum aldolase were detected already before clinical manifestations of the disease appeared.

"4. Among a group of 266 adult patients and 76 child patients with other diseases than IH serum aldolase values typical for IH were detected in 20 cases, i.e. in less than 6 per cent.

"5. When using the aldolase test in the epidemiology of IH, results can be expected only when the blood samples are taken at a suitable time, i.e. during the first days of the still undiagnosed disease. It may prove helpful also in examinations of persons in the focus of infection, where the disease is suspected.

"6. The significance of the considerable dispersal associated with the use of this method was discussed. If a single estimation is made, the result is not accurate enough to give an idea of the actual aldolase content of the serum.

"7. The authors recommend that several estimations of the same sample should be made simultaneously at every control examination and the average of these values should be used."

KIRK, R. **Virus Infections in the Sudan.** *J. Trop. Med. & Hyg.* 1959, Sept., v. 62, No. 9, 213–16. [14 refs.]

This is a brief review of the possible importance of several viruses in the Sudan. Antibody to Rift Valley fever virus has been found in human sera from the Nuba Mountains, but no further information is available. 626 sera from various parts of the Sudan were tested for antibody to West Nile virus: in samples of 16–45 sera from different places, antibody incidence ranged from 0 to 88% [this *Bulletin*, 1942, v. 17, 895; 1953, v. 28, 873; 1954, v. 29, 681]. Sera from "obscure neurological cases in Khartoum" and from 15 normal *Cercopithecus aethiops* monkeys were tested for antibody to encephalomyocarditis virus, but all were negative. 132 human sera from 5 localities were tested for Sindbis antibody—positive sera were found in 4 of the 5 places, the highest incidence being 30%.

C. E. Gordon Smith

LONGSHORE, W. A., Jr., OTA, Margaret I., HOFFMAN, Marjorie N., FUJIMOTO, Frances Y. & LENNETTE, E. H. **Transplacental Passage of Antibody to Western Equine and St. Louis Encephalitis Viruses.** *Amer. J. Trop. Med. & Hyg.* 1959, July, v. 8, No. 4, 424–32, 2 figs. [15 refs.]

Sera were collected from 1,009 mothers and their infants (cord blood) in an endemic area for western equine (WEE) and St. Louis encephalitis (SLE). As far as possible they were tested for complement-fixing and neutralizing antibody to the 2 viruses. Neutralizing indices of 1·0 log or more were considered positive as was a titre of $\frac{1}{8}$ or more in the complement-fixation test. 8 of 1,009 mothers had complement-fixing and 110 of 1,008 (there was insufficient serum for test on 1 individual) had neutralizing antibody to WEE; 31 of 1,009 had complement-fixing and 270 of 997 neutralizing antibody to SLE. Complement-fixing antibody was not found in the absence of neutralizing antibody. The incidence of neutralizing antibody increased with the duration of residence in the area: for WEE from 8% of those with less than 5 years' residence to 19% of those with 10–19 years' residence; the incidence of SLE antibody similarly increased from 15 to 37%. The maximum incidence of SLE antibody was 51% after 25–29 years' residence compared with 16% with WEE antibody in the same group.

All of 6 infants whose mothers had WEE complement-fixing antibody also had antibody, as did all of 25 infants whose mothers had SLE complement-fixing antibody. All of 110 infants whose mothers had WEE neutralizing antibody also had antibody as did 257 of

270 infants whose mothers had SLE neutralizing antibody. A few infants had antibody whose mothers did not, but these were of low titre and probably attributable to experimental error. The rate of disappearance of neutralizing antibody in the infants was followed by serial bleeding where possible. 30% of infants with WEE antibody had lost it at 3 months, 45% at 4 months, and 85% at 7 months. 75–85% of infants with SLE antibody had lost it at 6 months and practically all at 12 months. There appeared to be no difference in the rate of loss of WEE and SLE antibody so that the investigation failed to explain why 52% of cases of WEE are aged under 1 year compared with less than 1% of SLE cases in California [see also this *Bulletin*, 1956, v. 31, 1072]. *C. E. Gordon Smith*

HOLMGREN, B., LINDAHL, J., VON ZEIPEL, G. & SVEDMYR, A. **Tick-Borne Meningoencephalomyelitis in Sweden.** *Acta Med. Scandinavica.* 1959, Aug. 31, v. 164, No. 6, 507–22, 5 figs. [35 refs.]

This is a study of 240 patients with abacterial meningitis, meningoencephalitis or poliomyelitis of whom 176 were studied serologically. 68 of these had neutralizing and complement-fixing antibody against the Russian spring-summer group of viruses. A significant rise in antibody titre was demonstrated in 30 patients.

Estimates of the incubation period from the history of tick bite were 2–21 days with a mean of 7 days. 70% of patients had a biphasic illness. The first phase which resembled influenza lasted 2–12 days (mean 7 days) and was followed by an asymptomatic interval of 1–23 days (mean 8 days). The second phase had a sudden onset of fever, severe headache, neck rigidity, nausea, and vomiting. The fever lasted 10–12 days. Disturbances of sleep and mental imbalance were common. Tremors were frequent and cerebellar disorders occurred in some patients. Myalgia was common and about $\frac{1}{4}$ of cases had flaccid paralyses. Electroencephalograms revealed abnormalities in 70–80% during the first week, but most returned to normal by the end of a month. The cerebrospinal fluid showed increases in cells to less than 100 per cmm. in about $\frac{3}{4}$. The protein was raised but glucose normal. In 3 cases the cerebrospinal fluid was normal at a first examination, but abnormal 1 week later. $\frac{2}{3}$ of patients had a leucocytosis, usually polymorphonuclear.

Most patients were in hospital for 3–4 weeks and convalescence lasted 2–14 months (mean 5 months). Only 1 patient died and a post-mortem revealed encephalitis with large thromboses of cerebral arteries. Acute endomyocarditis and acute kidney infarction were also found. *C. E. Gordon Smith*

LACHMAJER, Jadwiga. **Fleas of Small Mammals in Natural Focus of Tick-Borne Encephalitis in the Puszcza Bialowieska (National Park).** *Bull. Inst. Marine Med. Gdańsk.* 1959, v. 10, Nos. 1/2, 5–14, 1 graph.

Fleas were collected from animals trapped in 3 types of forest as well as in cultivated land and around houses. 2,016 small mammals of 20 species were examined. 16 species of flea were taken. 61% of the *Clethrionomys glareolus* and 55% of the *Apodemus flavicollis* were infested. In drier forest these two rodents predominated but in humid marshy forest larger numbers of *Sorex* and *Neomys* spp. (*Insectivora*) were found. The hosts and seasonal population fluctuations of the main flea species are discussed in detail. 950 fleas were examined virologically and 2 strains of tick-borne encephalitis virus isolated. [This is mentioned only in the Conclusion, no details are given and the reference cited is WHO 1958 Euro 180/7.]

C. E. Gordon Smith

SKIERSKA, Barbara. **Culicidae in a Focus of Tick-Borne Encephalitis in the Puszcza Bialowieska (National Park).** *Bull. Inst. Marine Med. Gdańsk.* 1959, v. 10, Nos. 1/2, 15–29, 3 graphs. [15 refs.]

By using human bait, 24,219 mosquitoes of 21 species were caught in various types of forest. Practically all were caught between the end of May and the beginning of September. 32% were *Aëdes annulipes*, 26% *A. communis* and 23% in 6 other *Aëdes* spp. The relative incidence of different species at different times varied. The maximum attack rate recorded was 1,208 mosquitoes caught on one person in one hour. Mosquitoes were also caught using immobilized rodents as bait: 381 mosquitoes were caught on 28 *Apodemus flavicollis* and 432 on 36 *Clethrionomys glareolus*. Practically all were *Aëdes spp.*, *A. communis* being commonest (37%). In cultivated woods the picture was similar but numbers of mosquitoes were lower.

In a settlement, *A. cinereus* (24%), *A. annulipes* (19%) and *A. excrucians* (15%) were commonest. Peak biting activity was from just before dawn until about 4 hours after; there was a much lesser peak just before dark. Few (63) mosquitoes were caught inside dwellings: *A. communis* (25%) and *A. intrudens* (24%) were commonest, with *Culex pipiens molestus* predominating in the autumn.

Of 5,049 mosquitoes caught in stables and cowsheds 95% were *Anopheles* spp.

5,999 mosquitoes were processed for virus isolation and 5 strains were isolated from *Aëdes* spp. and one from *Anopheles maculipennis*. One of the *Aëdes* strains has been identified as tick-borne encephalitis virus. [No details are given and this information appears only in the Conclusions. The reference given is to PRZESMYCKI *et al.*, WHO Copenhagen, 1958.]

C. E. Gordon Smith

WEGNER, Zofia. **Lice on Small Mammals in a Natural Focus of Tick-Borne Encephalitis in the Puszcza Bialowieska (National Park).** *Bull. Inst. Marine Med. Gdańsk.* 1959, v. 10, Nos. 1/2, 31–8.

Of 2,016 mammals of 20 species only 85 animals of 11 species were infested with lice. 65 of the infested animals were *Clethrionomys glareolus*, less than 10% of the 732 *C. glareolus* examined. 6 species of lice were collected: *Hoplopleura acanthopus*, *H. longula*, *H.*

affinis, Polyplax gracilis, P. serrata and *Schizophthirus pleurophaeus*. Details of hosts, etc. are given. *C. glareolus* was about 10 times as heavily infested in humid forest which is flooded for months in the year, than in dry forest.

100 *H. acanthopus* were processed for virus isolation without success. *C. E. Gordon Smith*

i. Berry, J. N., Bidwai, P. S. & Junnarkar, R. V. **An Epidemic of Acute Encephalitis in Nagpur.** *J. Ass. Physicians India.* 1959, July, v. 7, No. 4, 333–46.

ii. Berry J. N. & Bidwai, P. S. **Aetiology and Epidemiology of Nagpur Epidemic of Acute Encephalitis.** *Ibid.*, 347–54, 2 maps & 2 graphs. [22 refs.]

These 2 papers contain a long account of an epidemic of acute encephalitis that occurred in Nagpur in July of 1958. In all 112 cases were admitted to the Medical College Hospital in Nagpur and there were 47 deaths. The clinical features of the encephalitis are presented in detail. The disease was equally prevalent in males and females but 70% of the cases were in children between 0 and 5 years of age. The cause of the epidemic was not determined but it was thought that it might have been due to a virus that was water-borne. Similar epidemics were occurring in other parts of India at about the same time, notably in Lucknow, and Drs. Pandit and Work, respectively Director of the Indian Council of Medical Research and Director of the Virus Research Centre at Poona, were actively engaged in investigating the aetiology of the disease. A report of their findings will probably be available later. *A. J. Beale*

Edge, W. E. B. **Acute Aseptic Meningitis: A Review.** *South African Med. J.* 1959, Aug. 22, v. 33, No. 34, 697–700. [32 refs.]

This is a clinical review of the subject. Possible causes are listed and 9 interesting case histories are given. [There is nothing new in this article: it is concise and up-to-date.] *A. B. Christie*

Čulik, J. & Zimák, V. Meningoencephalitis exanthematica. [**Exanthematic Meningoencephalitis**] *Časopis Lékařů Českých.* Prague. 1959, June 5, v. 98, No. 23, 717–21. [24 refs.] English Summary.

In January 1957 a number of cases of meningoencephalitis associated with an exanthem occurred in Ustí nad Labem, Czechoslovakia, and the histories of 4 cases observed by the authors are described. The onset was acute, with fever, headache and limb pains, a scarlatiniform exanthem on the trunk and limbs and signs of meningeal irritation. In 1 patient the course of the illness was biphasic. Attempts to isolate a virus in HeLa and monkey kidney cell cultures and in infant mice were unsuccessful. *D. J. Bauer*

Jumatov, H. J., Farizov, M. H., Kostina, K. A., Berezin, F. B., Preatkin, S. K., Reşetnikova, E. K., & Oleinik, P. F. Caracterizarea clinico-epidemiologica a encefalitei de Leninogorsk. [**Clinical and Epidemiological Findings in Leninogorsk Encephalitis**] *Studii şi cercetări Inframicrobiol.* 1959, v. 10, No. 1, 19–29. French summary.

The following is a translation of the French summary.

The authors describe a distinctive epidemic of encephalitis which they call Leninogorsk encephalitis after the locality in which it occurred. The first cases appeared in winter and early spring in schoolchildren and thereafter the disease spread to the rest of the population. The symptomatology included indisposition, asthenia, catarrh of mucous membranes, low fever, vertigo, nausea and vomiting; one patient in 5 showed somnolence. The commonest neurological symptoms were nystagmus, difficulty in convergence, abolition of abdominal reflexes, presence of abnormal pyramidal reflexes.

The course of the disease was benign except in a few cases in which neurological effects, especially subjective phenomena, persisted for 4–5 months.

In attempts to isolate a pathogenic agent various specimens taken from patients during the acute stage (blood, naso-pharyngeal washings, faeces) were inoculated into different laboratory animals, but without result. On the other hand 68 specimens of naso-pharyngeal washings and 6 of faeces were cytopathogenic for human embryo tissue cultures. These strains were neutralized by convalescent serum from patients who had had the disease, and bore no relation to influenza virus A2—1957.

In view of the clinical and epidemiological features the authors discuss the possible relationship between this disease and the encephalitis of von Economo (encephalitis lethargica). *Charles Wilcocks*

Lou, Fang-Ts'en. **Infectious Mononucleosis. A Review of 572 Cases.** *Chinese Med. J. Peking.* 1959, Aug., v. 79, No. 2, 175–7. [13 refs.]

This disease was first recognized in China in 1910 when an epidemic occurred in a seaport, Swatow. It has been reported from 5 different localities since that year, and the author describes the 6th, drawing his material from a study of 572 patients investigated in hospitals in Shanghai, during an epidemic which occurred in 1954–55. The disease made its appearance in October, rapidly reached a peak in November–December and declined abruptly from the end of February. The infectivity appears to have been high, and an illustration of this was provided by a technical college with a staff and student body numbering 1,267 persons, among whom 96·7% developed the disease in some form within a period of 1 month. The author quotes from a paper published in Chinese by Lou and Yeh (*Nat. Med. J. China*, 1958, v. 44, 939).

While overt manifestations of infectious mononucleosis were usually confined to patients below the age of 25 years, subclinical examples, which exceeded the former by 3 : 1, were largely discovered in those

above this age. The inference is that the adult population had, from previous experience of the infection, a residual degree of acquired immunity. Since the epidemic here described, only rare sporadic examples of the disease have appeared in the population of Shanghai, suggesting that a high degree of herd immunity has been re-established.

The disease showed 3 phases, prodromal, progressive and convalescent, and ran its course in 1–2 weeks. The clinical manifestations were so diverse that the author has described 11 different types and a 12th asymptomatic group. Certain features were observed in this epidemic in addition to those well known from western medical literature; these compromised a higher incidence of acute onset and of gastro-intestinal symptoms, also of generalized lymphadenopathy, and the occurrence, though rarely, of parotitis and epididymo-orchitis.

The author makes special mention of a pneumonic type of the disease and describes the varied radiological appearances. Among 21 such patients were seen mottled, snow-flake or gauze-like opacities, and occasionally large shadows resembling cumulus cloud. Exaggeration of normal marking [due to lymphatic engorgment], pleural reaction and even effusion were also noted. The thin gauze-like shadow often stretching across lobar boundaries was the most frequent finding. [To the reviewer this suggests pleural thickening rather than an intrapulmonary lesion.] Special attention was also paid to liver function in those patients in whom clinical evidence of liver involvement was evident. Even when such patients were anicteric quantitative changes in gamma globulin indicative of liver cell damage were demonstrated. In treatment, a range of sulphonamides and antibiotics all proved ineffective.

The haemotological changes noted included a moderate leucocytosis during the first 2 days with a return towards normal over the next 2 days. The polymorphs showed a shift to the left which was sometimes marked. The lymphocytes increased to an absolute figure of 3,000–4,000 per cm. after the 4th day, but this limited increase, which did not exceed 50% of the total leucocytes, was characteristic of the epidemic form of the disease and served to distinguish it from the sporadic variety in which a much higher relative lymphocytosis prevailed. The morphological abnormalities of the lymphocytes characteristic of the disease were observed to persist for at least 2 months. The concentration of erythrocytes, haemoglobin and platelets was not disturbed.

Heterophil antibodies at a titre exceeding 1 : 64 were found in 96·4% of all patients, and these resisted cross absorption in 86·5% of specimens. Even then ox cells did not absorb all antibodies completely for in ¾ of the sera residual agglutinins to sheep cells remained, suggesting that a wide antibody response had been evoked. The titre of heterophil antibodies bore no relationship to the clinical severity of the disease. Cold agglutinins and false positive Kahn and Wassermann reactions developed transiently in a few patients.

All attempts to isolate a causal virus were unavailing even after serial blind passage in mice. A single autopsy is described in which there was found widespread necrosis of parenchymal cells in many organs, together with multiple haemorrhages and marked mononuclear cell infiltration.

[This paper bears witness of the skill and thoroughness of modern Chinese hospital practice.]

J. H. Walters

DODDS, E. J. A. **A Case of Glandular Fever causing Respiratory Obstruction.** *Practitioner.* 1959, May, v. 182, No. 1091, 595–7.

A child (age not given) was on the waiting list for removal of tonsils and adenoids when he developed what was apparently a recurrence of sore throat. He rapidly developed severe dyspnoea requiring laryngeal intubation followed by tracheotomy. The author considered that his nasopharyngeal obstruction was due to a combination of upper respiratory tract infection, enlarged tonsils and glandular fever: white cell counts and Paul Bunnell test supported the diagnosis.

A. B. Christie

HYMAN, R. A. **Acute Haemolytic Anaemia complicating Infectious Mononucleosis.** *Practitioner.* 1959, May, v. 182, No. 1091, 615–17.

One week after the onset of infectious mononucleosis the patient, a boy aged 16, developed haemolytic anaemia: haemoglobin was 6·5 gm.%, reticulocytes 39·4%, and red cell fragility normal; sternal marrow showed erythroid hyperplasia, the direct Coombs test was negative and no auto-antibodies active at 37°C. or in the cold were present. The patient recovered without specific treatment. Possible mechanisms behind the haemolysis are discussed including the haemagglutinating activity of a virus, hypersplenism, drug reaction or the production of haemolytic immune antibodies.

A. B. Christie

MUSCHEL, L. H. & PIPER, D. R. **Enzyme-Treated Red Blood Cells of Sheep in the Test for Infectious Mononucleosis.** *Amer. J. Clin. Path.* 1959, Sept., v. 32, No. 3, 240–44. [10 refs.]

The antibody that reacts with infectious mononucleosis serum is released from sheep red cells, or inactivated, by exposing the cells to various enzymes. This paper correlates the enzyme effect with the established absorption methods in the Paul-Bunnell test, with the object of making the test more specific.

In the standard test, when sera from patients with glandular fever are absorbed with guineapig kidney, and then tested against untreated sheep cells, a reduction of agglutinin titre to a half is common, and to a quarter is not unusual. In the authors' 13 cases of proved glandular fever, this partial absorption was seen in 12 out of 17 tests. But when guineapig kidney was replaced by papain-treated sheep erythrocytes as the absorbing agent, there was no reduction in titre in any test. However, the same process applied to sera containing heterophil agglutinins *not* due to glandular fever resulted in complete removal of the agglutinins active against normal sheep erythrocytes.

Further, when papain-treated sheep cells were used as the antigen when testing the unabsorbed sera of

true cases of glandular fever, the titres recorded were less than with untreated erythrocytes; by contrast, in 4 patients with heterophil agglutinins not due to glandular fever the enzyme-treated cells gave titres up to 8 times those given by untreated cells.

The use of enzyme-treated cells, both as test cells and as absorbing agents, thus enhances the specificity of the heterophil agglutinin test. *Alan B. Raper*

IPPEN, H. Mesantoinschädigung und Mononucleosis infectiosa. [**Toxic Effects of Mesantoin and Infectious Mononucleosis**] *Deut. med. Woch.* 1959, Apr. 3, v. 84, No. 14, 673–4, 683–6, 708, 5 figs. (4 on 2 pls.) [55 refs.]

In this paper the author says that its title may appear to be surprising in linking the toxic effects of mesantoin with infectious mononucleosis. There are, however, similarities between the 2 conditions, illustrated here by a clinical case and by a number of references to the literature, which make the differential diagnosis of much importance.

The clinical case was a mycotic dermatitis of the legs with scattered lesions over the rest of the body in a woman 44 years of age who was admitted to hospital where, because of positive evidence of epilepsy she was treated with 0·1 gm. Mesantoin (Sandoz) (3-methyl-5-ethyl-5-phenylhydantoin) 4 times daily [the English summary gives the dose as 0·5 gm. 4 times daily but this is wrong]. There is a description with photographs of the skin lesions for which she was admitted and of their treatment. After 16 days of mesantoin treatment, however, a papular eruption and a punctate rash developed, the submandibular and cervical lymph nodes enlarged and there was swelling of the nose. The blood picture showed the presence of atypical mononuclear cells. Her condition deteriorated in spite of cessation of the mesantoin treatment, the rash became extensive and the glands more enlarged and there were periods of fever. Treatment with corticoids was then begun and was at first followed by an improvement in the patient's condition but later by a relapse in which there was fever, marked facial oedema and bleeding from the gums. There was a blood picture of a leucocytosis of 28,700 with 38% eosinophilia and many atypical mononuclear cells. In a long discussion the view expressed is that infectious mononucleosis can be excluded because of the marked eosinophilia and negative Paul-Bunnel test and that the case was one of mesantoin poisoning. *M. E. Delafield*

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

FAGUET, M. Enregistrement des courbes de croissance microbienne par le microbiophotomètre électronique. [**Recording of Bacterial Growth-Curves by means of an Electron-Microbiophotometer**] *Ann. Inst. Pasteur.* 1959, Aug., v. 97, No. 2, 177–87, 8 figs.

This paper describes an apparatus designed to give continuous photometric measurements of microbial growth over extended periods. The culture vessels are mounted on a rotating stand and each culture passes once a minute between a light source and a photo-electric cell. The electromotive force generated by the cell is balanced by an automatic electronic potentiometer so that no current flows in the photo-electric cell circuit at the point of measurement. When the culture passes between the light source and the cell the EMF alters and the change in EMF is registered on a paper strip and gives a measure of the opacity of the culture. With the instrument described it is possible to compare the growth curves of 6 microbial cultures to which different physical or chemical conditions apply. *R. B. Morrison*

GOLLUB, Edith G. & GOTS, J. S. **Purine Metabolism in Bacteria. VI. Accumulations by Mutants lacking Adenylosuccinase.** *J. Bacteriology.* 1959, Sept., v. 78, No. 3, 320–25, 5 figs. [20 refs.]

CONTOIS, D. E. **Kinetics of Bacterial Growth: Relationship between Population Density and Specific Growth Rate of Continuous Cultures.** *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 40–50, 5 figs. [16 refs.]

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; Colicines; Other Therapeutic Substances; Disinfection.**

De Felip, G., Alberti, Silvana & Von Lorch, Littoria. Titolazione rapida degli antibiotici mediante l'impiego della resazurina. [**A Rapid Method of Titrating Antibiotics by the Use of Resazurin**] *Rendiconti Istituto Superiore di Sanità.* Rome. 1959, v. 22, Pt. 5, 534–42. [14 refs.] English summary (6 lines).

A modification is described of a method for titrating antibiotics, first described by Pital *et al.* [this *Bulletin*, 1956, v. 31, 1033], depending on the reducing action of bacterial growth on resazurin and the change in colour from blue to red, no such change occurring where bacterial growth had been inhibited.

6 ml. of medium suitable for the micro-organism being used and seeded with it were poured on plates containing 20 ml. of plain agar. To this had also been added, when it had been cooled to 45°C., 0·1 ml. of a 1% solution of resazurin. This solution has to be recently prepared as it does not keep well even at 4°C. The inoculum consisted of 0·15 to 0·20 ml. of an 8-hour broth culture of the test organism diluted 1 in 10. Cylinders containing the antibiotic being tested [8 antibiotics were used] were set on the agar, plates being incubated at 37°C. and observed for 24 hours. Control tests in which the indicator was omitted were carried out. Most antibiotics could be titrated in 3 to 6 hours. Results could be read very clearly, although the colour differences did not persist for 24 hours, when only the growth inhibitions could be seen. The diameters of the inhibition areas were always proportional to the amount of antibiotic used. This method was tested on *Sarcina lutea, Bacillus subtilis, Micrococcus pyogenes var. aureus, Esch. coli, Brucella bronchiseptica, Micrococcus flavus, Strep. faecalis,* and *Klebsiella pneumoniae.* The growth of *M. flavus* was inhibited by the amount of resazurin used and this did not appear to be a suitable organism for this work. In titrating polymixin B sulphate using with *Brucella bronchiseptica*, readings could only be made after 10 hours through the characteristically slow metabolism of the micro-organism. *E. Agius*

Balan, J., Ebringer, L, Nemec, P. & Šatura, D. Ein neuer Rohstoff für die Erzeugung von Antibiotika, insbesondere des Penicillins. [**A New Material for the Production of Antibiotics, Particularly Penicillin**] *Zent. f. Bakt.* II. Abt. 1959, Sept. 25, v. 112, Nos. 21/25, 715–21, 6 figs.

Medical J. Australia. 1959, June 20, v. 1, No. 25, 827–30. **Report on a Survey of Allergic Reactions to Penicillin.** An Investigation conducted by the Research Committee of the N.S.W. Faculty of the Australian College of General Practitioners.]

The information analysed here was supplied by 36 doctors. It relates to the treatment with penicillin of 6,832 patients, of whom 88 (1·3%) developed a reaction. These included 60 males and 27 females (but since the sex of 1,526 patients was not stated, the sex ratio for total numbers treated remains conjectural). An immediate reaction occurred in 7, 1 having severe shock, 5 lesser degrees of shock and 1 urticaria. The features of the remaining delayed reaction (mainly skin manifestations) are analysed. Most of the reactions followed procaine penicillin, but this was given far more often than any other form: the percentage incidence of reactions after different forms was procaine 1·4, benzathine 3·8 (6 reactions in a total of 159 patients) "crystalline" 1·7, mixtures of these 2·0 and oral 0·5. A high proportion of the reactors had been given penicillin before (it would be interesting to have the same information for non-reactors): 3 with immediate and 7 with delayed reactions had reacted before, and 47 of the delayed reactors had personal or family histories of allergy. Inquiry on these matters before starting treatment is thought to be a valuable safeguard. The value of skin tests is discussed, mainly on the basis of other work, since in fact they were scarcely used at all in this study. *L. P. Garrod*

Konn, H [**Intrauterine Fetal Death caused by Anaphylactic Shock after Penicillin**] *Dapim Refuiim.* Tel-Aviv. 1959, Aug. v. 18, No. 3 [in Hebrew 136. English summary iv].

"A case is reported of a woman in the ninth month of pregnancy who had an anaphylactic shock immediately after an injection of penicillin for a small panaritium on a finger. After consciousness returned, labor pains started. She arrived at our hospital in the middle of her labor. There were no fetal heartbeats. Three hours later she delivered a freshly dead infant of 2650 gr. weight.

"The postmortem findings were typical for anoxia ('cyanosis, atelectasis of lungs subcapsular hemorrage of liver and hemoperitoneum, multiple petechiae of pleura and pericard.').

"There is no doubt, that the death of the child was caused by anoxia due to anaphylactic shock of the mother after penicillin."

Knothe, H. & Mahler, J. Untersuchungen *in vitro* und *in vivo* über die Bedeutung hoher Tetracyclin-Blutspiegel. [*In vitro* **and** *in vivo* **Studies on the Significance of High Tetracycline Concentrations in Blood**] *Deut. med. Woch.* 1959, Sept. 11, v. 84, No. 37, 1687–9, 1715–16, 3 figs.

These authors from Kiel administered tetracycline orally or pyrrolidine methyl tetracycline intravenously to dogs and rabbits, each in a single dose of 20 mgm./kgm., and at intervals thereafter estimated the amount of antibiotic in the blood and other body fluids and in

various organs. The intravenous form produced much higher levels in the blood, which were well sustained: *e.g.*, after 6 hours 5·8 and 13·8 μgm./ml. were found in the blood of dog and rabbit respectively, whereas at this time after oral administration the amounts found were 0·7 and <0·1 mgm./ml. The amounts in urine, bile, liver, kidney and muscle were also consistently much higher after the intravenous dose. [The fact that so little was excreted in either urine or bile after the oral dose seems only explicable by grossly inadequate absorption.] Estimations were also made in aqueous humour, brain, lung, spleen and bone.

The paper begins by describing some *in vitro* experiments designed to show that high blood levels are useful. Broth inoculated with *Staphylococcus aureus*, *Escherichia coli* or *Streptococcus faecalis* and containing 25 μgm./ml. of tetracycline, was progressively diluted with fresh medium to imitate a falling concentration in the blood: serial viable counts up to 24 hours nevertheless showed a bactericidal effect, particularly during the first 8 hours (a fall from about $10^{6·5}$ to $10^{3·5}$/ml. in one example given). In contrast, an unchanging concentration of 2·5 μgm./ml. had little more than a bacteriostatic effect. *L. P. Garrod*

Dimmling, T., Gerlach, J. & Simon G. Die Tetracyclinkonzentration im Liquor unter besonderer Berücksichtigung von Pyrrolidino-methyl-tetracyclin. **[Tetracycline and Pyrrolidine - Methyl - Tetracycline Concentration in Cerebro-Spinal Fluid]** *Deut. med. Woch.* 1959 Sept. 11, v. 84, No. 37, 1689–93, 1716, 4 figs.

Patients subjected to cranial surgery were given 1 gm. tetracycline intravenously as cover for the operation, and its concentration was determined in blood and cerebrospinal fluid at various intervals up to about 30 hours. As the blood concentration fell, that in the fluid rose, reaching 1–2 μgm./ml. in the middle of this period: at the end of it the two levels were approximately the same. Similar studies were made in patients given repeated doses of 250 mgm. of pyrrolidine-methyl-tetracycline at 24-hour intervals either intravenously or intramuscularly. Injection by the latter route gave distinctly lower levels in both blood and cerebrospinal fluid: after intravenous injection these were satisfactory, but, as the authors say, they cannot be compared directly with those produced by giving tetracycline, since the dosage was different.
L. P. Garrod

Graf, H. & Riemann, S. Untersuchungen über die Konzentration von Pyrrolidino-methyl-tetracyclin in der Muttermilch. **[The Concentration of Pyrrolidine-Methyl-Tetracycline in Breast-Milk]** *Deut. med. Woch.* 1959, Sept. 11, v. 84, No. 37, 1694–7, 1716, 5 figs. [32 refs.]

The concentration of tetracycline in breast milk was determined after giving this antibiotic in 2 different forms. Within 4 hours of a dose the concentration was higher at the end of a feed than at the beginning: further comparative observations were therefore made with milk obtained at the end. The highest levels (maximum about 2 μgm./ml. after 4 hours) were obtained by giving 275 mgm. pyrrolidine-methyl-tetracycline intravenously: the level fell slowly, about 0·3 μgm./ml. being still present after 24 hours, and that in the milk slightly exceeding that in the blood from the 8th hour onwards. [These figures are only approximate: several series of tests were done, apparently with somewhat different results.] The same form of tetracycline given intramuscularly produced slightly lower levels, and a dose of 250 mgm. tetracycline phosphate complex orally gave much lower levels (about one-third of the foregoing). When intravenous pyrrolidine-methyl-tetracycline was given daily for 3 days, there was no cumulative effect in the milk. It is calculated that during such treatment the infant would receive 1·2 mgm. of tetracycline daily, an amount which is regarded as indifferent. [Puerperal mastitis is mentioned in the introductory sentence, and the data obtained are presumably thought to have a bearing on its treatment.] *L. P. Garrod*

Suzue, G. & Tanaka, S. **Carotenogenesis and Resistance of** *Micrococcus pyogenes* **to Tetracyclines.** *Science.* 1959, May 15, v. 129, 1359–60, 1 fig.

A strain of *Staphylococcus aureus* originally sensitive to 0·5 μgm./ml. of tetracycline or of oxy- or chlortetracycline was rendered resistant to 300 μgm./ml. and was observed to have lost its pigment. Extraction confirmed the total absence of carotenoids. It is suggested therefore that tetracyclines may interfere with the synthesis of these pigments. *L. P. Garrod*

Hirsch, H. A. & Finland, M. **Effect of Food on the Absorption of Erythromycin Propionate, Erythromycin Stearate and Triacetyloleandomycin.** *Amer. J. Med. Sci.* 1959, June, v. 237, No. 6, 693–709, 4 figs. [32 refs.]

This paper describes a study of the absorption of 3 antibiotic preparations in normal subjects. The findings are somewhat complicated by the use of 3 assay methods (tube dilution tests with *Staphylococcus aureus* and *Streptococcus pyogenes*, and a plate diffusion method with *Sarcina lutea*), and by expressing the findings both in terms of antibacterial activity of the serum and as the w/v concentration of each antibiotic. A strong plea is made for the adoption of the former convention, *i.e.*, for "comparing different antibiotics on the basis of the same standard of reference". [This may be preferable for closely related antibiotics such as those used here, but how different must they be to render the procedure inapplicable?] Observations were also made on the effects of the relation of a dose to a meal.

In the first experiment described doses of 500 mgm. of erythromycin propionate and triacetyloleandomycin respectively were given to 2 groups of men at 9.0 a.m. and 9.0 p.m. for 7 days: the antibacterial activity of the blood differed little in the 2 groups and the absolute concentration of oleandomycin in the blood was higher than that of erythromycin. In further tests single 500 mgm. doses were given either before or

after breakfast. Triacetyloleandomycin was well absorbed when given either before or after a meal, but the absorption of erythromycin propionate and erythromycin stearate was much reduced when they were given after a meal. Much the highest levels of antibacterial activity of all those recorded were obtained by giving erythromycin on a fasting stomach: of the 2 forms the propionate gave the higher level.

[See also this *Bulletin*, 1959, v. 34, 922.]

L. P. Garrod

ALBRIGHT, J. G. & HALL, W. H. **Triacetyloleandomycin: A Study of Blood Levels and Clinical Effects.** *Antibiotic Med.* New York. 1959, May, v. 6, No. 5, 283–8, 2 figs.

A single 500 mgm. dose of each of 4 antibiotics was given at different times to 9 normal subjects, and the antibiotic concentration in the blood was determined 2 hours later by the *Sarcina lutea* cylinder plate method. The average amounts found in μgm./ml. were triacetyloleandomycin 1·83, propionyl erythromycin 1·38, oleandomycin 0·98, erythromycin 0·2. Expressed as erythromycin equivalents (*i.e.* in terms of antibacterial activity, and not in w/v concentration for each antibiotic) [this *Bulletin*, 1959, v. 34, 922] these figures became 0·6, 1·4, 0·4 and 0·2 respectively, erythromycin having a greater activity against the test organism than oleandomycin.

Triacetyloleandomycin was given, usually in doses of 500 mgm. 4 times a day, for 7–10 days to 19 patients with urinary tract infections, 8 with wound infections, 5 with furunculosis and 7 with pneumonia. The results were good in infections caused by staphylococci or streptococci. The treatment was also successful in eliminating pathogenic staphylococci from the noses of 10 carriers among operating theatre personnel. Side effects, most commonly diarrhoea, were caused in 15 (28%) of a total of 53 persons treated.

L. P. Garrod

LECCA, G. G., TERRY, J., MAGGIOLO, L. & MORALES, A. **Ototoxicity of Kanamycin. Report of Three Cases.** *J. Amer. Med. Ass.* 1959, Aug. 22, v. 170, No. 17, 2064–8, 4 figs. [13 refs.]

This paper is from the British American Hospital, Lima, Peru. 3 patients given kanamycin developed severe and apparently permanent hearing loss. A man aged 46 was given 40 gm. in 16 days for treatment of (apparently local) peritonitis after a gastrectomy; a subphrenic abscess containing staphylococci was drained later. The blood urea, originally normal, is recorded as having risen to 140 mgm.% on 2 occasions during the course of treatment. A man aged 62 had had repeated attacks of urinary infection since childhood and a nephrectomy for stones 12 years before: his initial blood urea was 170 mgm.%. He received 14 gm. in 7 days for his urinary infection. The third case was a woman aged 55 with an initial blood urea of 68 mgm.% and red cells and casts as well as *Escherichia coli* in her urine (whether it contained albumin is not mentioned), who also received 14 gm. in 2 short courses. The deafness, which is described as total in the first and third cases (audiograms are reproduced), developed during the last day or two of the course or immediately after it. [The authors do not conclude that kanamycin should not be given to any patient with impaired renal function, but this would seem to be a wise deduction from their experience, and is an accepted principle in connexion with the use of neomycin, a closely related antibiotic.] *L. P. Garrod*

HERTMAN, I. & BEN-GURION, Renana. **A Study on Pesticin Biosynthesis.** *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 135–43, 3 figs. [10 refs.]

"Strains of *Pasteurella pestis* under certain conditions form a bacteriocin-like material, which has been named pesticin. Pesticin formation was induced by ultraviolet irradiation. A chemically defined medium composed of inorganic salts and amino acids supported the synthesis of pesticin by irradiated organisms. The mimimal amino acid requirement for pesticin synthesis has been established. For the synthesis of pesticin at 37° the irradiated organisms required certain amino acids which they did not require at 27°. Bacteria in the stationary phase and actively dividing bacteria were equally able to produce pesticin upon irradiation. Concentrations of chloramphenicol lower than those required for bacteriostasis inhibited pesticin synthesis. Non-pesticin producing mutants of *P. pestis* were obtained by exposure of the bacteria to higher doses of u.v. irradiation than those required for the induction of pesticin formation. These mutants were sensitive to pesticin."

[See this *Bulletin*, 1959, v. 34, 475.]

VIEU, J. F. Recherche et numération des bactéries colicinogènes. **[Isolation and Enumeration of Colicinogenic Bacteria]** *Ann. Inst. Pastuer.* 1959, July, v. 97, No. 1, 117–20.

Employing the double agar layer technique [GRATIA *et al.*, this *Bulletin*, 1950, v. 25, 950] the author has studied the reciprocal antibiotic activities of aerobic bacteria, particularly those active against the coliform bacteria. From the same stool 3 preparations were made: a dense faecal suspension in distilled water and 2 broth cultures which were not aerated or agitated; one of these was incubated for 6½ hours and the other for 18 hours. Various dilutions of these preparations were added to melted agar to form the lower layer in the special double layer technique. When these plates were cooled and the agar well set the second layer of agar was poured, and allowed to set. The plates were then incubated for 48 hours, after which each surface was sown with the indicator strain, *Escherichia coli* K 12, and further incubated for 18 hours at 37°C. The next day varying numbers of circular areas of growth inhibition of K 12 could be seen centred over a bacterial colony in the lower layer from which the antibacterial substance had originated and diffused through the agar layer to reach the surface. It was thus possible to identify and count the colicinogenic bacteria in the particular specimen of faeces.

H. J. Bensted

BAVASTRELLI, L. Richerche sulle proprietà colicinogene e sulla sensibilità a varie colicine di stipiti di colibacilli iso'ati da gastroenteriti infantili. [**Research on the Colicinogenic Properties and on the Sensitivity to Various Colicines of Coliform Bacilli from Cases of Infantile Gastroenteritis**] *Riv. Istituto. Sieroterap. Ital.* 1959, May–June, v. 34, No. 3, 172–83, 1 fig. [29 refs.] English summary.

Colicines appear to act by a preliminary fixation on the sensitive micro-organism which possesses special receptors. There are various types of colicines acting specifically on bacteria which can also produce mutants resisting one type of colicine but not another. They appear to be polypeptides and identical or closely associated with O antigen. Their action is bactericidal.

In this investigation the power of producing colicines and the sensitivity to them in a group of coliform bacteria from various human sources were studied with the object of discovering any correlation with the antigenic structure especially of those of the serologically defined pathogenic *Escherichia coli*. It was also hoped this might reveal epidemiological connexions.

Among 235 strains of *E. coli* coming mainly from cases of infantile gastroenteritis belonging to the known O pathogenic types and to some unidentified types, 42 were found to be producers of colicine; 26 of these produced colicine of type A, B, D and E, while the colicines from another 16 strains could not be identified. Colicines derived both from the identified and the unidentified *coli* types. Among 17 colicinogenic strains in type O 25, 11 produced colicine type B. This correlation in colicinogenicity ran parallel with biochemical and serological properties. 4 other strains of O 25 producing different colicines, also differed in their other properties.

The studies on sensitivity of strains to colicines were not conclusive except as far as showing that colicine D appeared to be the most widely active. Colicinogenic properties among the pathogenic strains are independent of the serological type, which was not unexpected since the somatic O antigen is common to various subtypes. Colicinogenic typing could therefore be used together with biochemical, serologic and phage-typing as a means of strain identification. *E. Agius*

BORICK, P. M., BRATT, M., WILSON, A. G., WEINTRAUB, L. & KUNA, M. **Microbiological Activity of Certain Saturated and Unsaturated Fatty Acid Salts of Tetradecyclamine and Related Compounds.** *Applied Microbiol.* Baltimore. 1959, July, v. 7, No. 4, 248–51. [12 refs.]

MELLAN, I. & LUBOWE, I. I. **Sanitizers based on Pine Oil.** *Soap.* New York. 1959, Apr., v. 35, No. 4, 74–5, 79, 105, 2 figs. [15 refs.]

This paper begins by explaining that pine oil is distilled from the stumps of felled pine trees which used formerly to be left in the ground: a formidable machine now used for uprooting these is illustrated. The properties of pine oil are described, and its "formulation" into disinfectants and soaps is discussed, the composition of several such products being stated. Various non-medical uses depending on its detergent, penetrating and cleaning properties are also mentioned. The only original observations reported were aimed at improving the bactericidal activity of household cleaning preparations containing pine oil, and consisted of testing the activity of such a preparation against 2 species each of bacteria and fungi after the addition of other constituents. The method used is not described, and the significance of the Tables of results is not clear, but the conclusion reached is that such a preparation can be improved by incorporating 0·5% of hexachlorophene in it. *L. P. Garrod*

THOMPSON, R. E. M. & O'GRADY, F. W. **An Improved Box for the Sterilisation of Dressings.** *Lancet.* 1959, Sept. 26, 445–6, 1 fig.

This article describes a new sterilizing casket which is the logical development of the Konrich drum, in which open air-ports closed by slides are replaced by perforations in the lid and base, permanently protected by a fabric filter, permeable to steam and air but not to bacteria. The casket is made of heavy gauge copper, and is rectangular (12 × 10 × 8 inches). The lid and base have each 1,216 perforations of $\frac{1}{8}$ inch diameter. A fabric filter is held against the perforations inside the casket and the filter material of the lid is extended to form a gasket which seals the casket when closed. A number of fabrics were tested for their suitability as filters. Heavy cotton twill (15–20 oz. per sq. yard) is cheap but discolours with use. Heavy nylon twill (10–15 oz. per sq. yard) was found to be more expensive but it did not discolour, it did not absorb moisture, it was very strong and it was immune to attack by bacteria.

The casket was tested for steam permeability by including thermometers and preparations of *Bacillus subtilis* spores in typical loads. All such tests were satisfactory. The long term maintenance of sterility was tested by autoclaving the casket and putting opened blood agar plates inside, half facing upwards and half downwards. The caskets were then placed in the trunking of a forced ventilating system. Plates in closed caskets were sterile on incubation after exposure for up to 2 weeks. Plates similarly exposed in a slide-type box were always contaminated after 3–7 days. Control plates exposed in the trunking were contaminated in 30 minutes.

Resistance to direct contamination was tested by pouring graded amounts of a broth culture of *Sarcina lutea* on to the outside of the filter and swabbing the inside 10 minutes later. Up to 0·5 ml. of culture was resisted by the filter, whereas 0·05 ml. penetrated a slide-type box under similar conditions.

In their discussion the authors point out the superiority of such caskets over standard containers closed by slides, and suggest that they may be preferable to fabric packs where conditions of storage and transport are bad.

[It is perhaps to be regretted that the tests for sterilization did not include chemical indicators or thermophilic spores. The debate concerning the best way of packing goods for sterilization continues—until more experience has been obtained no conclusion can be reached. It is unlikely that any one form of packaging will prove suitable for all loads in all circumstances.]

J. C. Kelsey

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

VANCURÍK, J. & ŠVEJCAR, J. Příspévek k mikrobiologické diagnostice stafylokoků—Sděleni II. Význam stanovení leukocidinu a jeho vztah k některým dalším vlastnostem stafylokoků. [**A Contribution to the Microbiological Diagnosis of Staphylococci—Communication II. The Importance of determining Leucocidin and its relation to some Further Properties of Staphylococci**] *Československ. Epidemiol., Mikrobiol., Immunol.* Prague. 1959, v. 8, No. 5, 304–16, 4 graphs & 3 figs. [22 refs.]

The English summary appended to the paper is as follows:—

"On two sets of (407 and 412 coagulase positive) staphylococci the authors verify the importance of leucocidin for the determination of the degree of pathogenicity and its relation to other ferments, to its susceptibility for antibiotics and its place in some group of bacteriophages. The following of leucocidin occurrence has been completed by investigation of 331 coagulase negative staphylococci.

"Obtained results confirm the possibility of selection of more dangerous strains of coagulase positive staphylococci by means of determining leucocidin. Strains from morbid lesions were positive in 67·6 p. c. of cases, carrier strains only in 17·2 p. c. of cases. Relatively unexpected was the detection of a high percentage of leucocidin producing strains obtained from the throat and nose of persons suffering from staphylococcal infection localized in some other part of their body. A comprehensible difference was found in leucocidin positiveness of strains isolated from carriers among hospital personnel (30·8 p. c.) and from carriers from supply departments (17·2 p. c.).

"Leucocidin positive strains were usually better furnished with ferments. 55 p. c. of leucocidin positive strains contained the four determined ferments in comparison with 23·5 p. c. leucocidin negative strains and conversely, in leucocidin positive strains we have found only one ferment in 4·3 p. c. of cases, whereas in leucocidin negative ones in 17·4 p. c. of cases. No prevalence of strains with leucocidin for some of the current phage groups was established. Leucocidin positive strains manifested greater resistance to antibiotics.

"No leucocidin was determined in any coagulase negative strains. Other followed components were found only very rarely and in minimal titres only with the exception of delta lysin which was proved in 8·1 p. c. of investigated strains.

"These facts underline the diagnostic importance of determining leucocidin which may become a valuable guide in evaluating staphylococcal strains."

RICHMOND, M. H. **The Differential Effect of Arginine and Canavanine on Growth and Enzyme Formation in *Staphylococcus aureus* 524 SC.** *Biochem. J.* 1959, Sept., v. 73, No. 1, 155–67, 10 figs. [Numerous refs.]

DRUMMOND, Margaret C. & TAGER, M. **Enzymatic Activity of Staphylocoagulase. I. Characterization of an Esterase associated with Purified Preparations.** *J. Bacteriology.* 1959, Sept., v. 78, No. 3, 407–12, 5 figs. [14 refs.] **II. Dissociation of Plasma Clotting from Tributyrinase Activity.** *Ibid.*, 413–21, 7 figs. [17 refs.]

KOCH, Marie L., KASTENSEN, Lorraine M. & RESNICK, A. **Report on Commonly Occurring Phage Patterns in a Hospital in which Staphylococcal Infections are Endemic.** *Antibiotics & Chemotherapy.* New York. 1959, July, v. 9, No. 7, 409–15. [15 refs.]

This paper reports the bacteriophage typing of 1,152 and drug sensitivity of 760 strains of coagulase positive strains of staphylococci isolated over a 14½ month period in a general hospital in Wisconsin. No epidemic was experienced during this time but the authors' definition of an epidemic is not given.

Only 66% of strains were typable. 50% at routine test dilution [RTD] and 16% with phages diluted 1/10. [This technique may account for the low percentage of typable strains. Some phage filtrates are 100,000 RTD and some only 1,000 RTD and different batches of individual phages may vary. An overall dilution of 1/10 may produce unreliable results. It is the usual practice to type strains non-typable at RTD, with phages at 1,000 RTD.]

59% of strains were included in 6 phage patterns and 39% fell into 2 patterns (53/VA4 and 80/81). 84·3% of 53/VA4 strains and 83·6% of 80/81 strains were resistant to several antibiotics but more 53/VA4 than 80/81 strains were resistant to erythromycin, dihydrostreptomycin and chloramphenicol.

The site of infection due to strains of the 6 common types is given. 69 of 102 respiratory tract infections and 61 of 126 surgical wounds were due to type 53/VA4,

and 53 of 82 boils were due to type 80/81, but factors such as ward distribution, surgical teams or other opportunities for cross-infection are not discussed.

The authors stress the fact that the majority of strains causing hospital sepsis fall into a few phage patterns [4 of the 6 patterns quoted here are also recognized as epidemic types in Britain.] *M. Patricia Jevons*

i. PAINE, T. F., Jr. & DANIEL, R. R. **Attempts to obtain Gram-Negative Rods from Staphylococci treated with Penicillin.** *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 203–4.

ii. BRIGGS, Shirley, CRAWFORD, Kathleen, ABRAHAM, E. P. & GLADSTONE, G. P. **Further Observations on the Relationships between Gram-Negative Rods and Staphylococci grown in the Presence of Penicillin.** *Ibid.*, 205–7.

iii. HILSON, G. R. F. & ELEK, S. D. **An Investigation into the Development of Gram-Negative Rods in Penicillin-treated Cultures of** *Staphylococcus aureus*. *Ibid.*, 208–20, 1 fig. [13 refs.]

i. "Gram-negative bacilli could not be obtained from the Oxford strain of *Staphylococcus aureus* nor from 15 other strains of *S. aureus* in the presence of benzylpenicillin."

[See Briggs *et al.*, this *Bulletin*, 1957, v. 32, 1089.]

ii. "It has not been found possible to repeat the work of Briggs *et al.* (1957) in which Gram-negative rods were isolated from cultures of staphylococci treated with penicillin, and staphylococci were subsequently recovered from cultures of these rods when the latter were grown in the absence of penicillin. No flaw in technique has been revealed which would enable the earlier results to be readily explained in terms of contamination."

iii. "Attempts were made to obtain Gram-negative rods from the Oxford strain of *Staphylococcus aureus* in the presence of benzylpenicillin. Two such isolations were made in 476 test cultures and one in 192 controls. The difference is not significant. No reversion to coagulase-positive staphylococci could be demonstrated of a rod-shaped Gram-negative organism previously reported as showing this effect. The question of the presence of Gram-negative rods in staphylococcal cultures exposed to penicillin is discussed and it is considered that the phenomenon is due to contamination."

ZANEN, H. C., GANOR, S. & VAN TOORN, M. J. **A Continuous Study of Hemolytic Streptococci in the Throats of Normal Children, Adults and Aged Men.** *Amer. J. Hyg.* 1959, May, v. 69, No. 3, 265–73. [13 refs.]

Fortnightly throat swabs were taken from 40 children in a home, 35 men in an old peoples' home and 22 laboratory workers, over a period of 30 months. Swabs were put into modified Pike's enrichment medium [this *Bulletin*, 1955, v. 30, 1021] and plated on blood agar plates containing crystal violet after 18 hours. Plates were incubated anaerobically. β-haemolytic streptococci so isolated were grouped and Group A strains were typed.

Results from the children's home showed that the isolation rate of group A streptococci varied from 3 to 100% and there were 7 major epidemics. 10–17% of infections produced clinical disease. Types 28, 4/26, 22, 12, 5/27/44 and 14 were the commonest types but only a few types (particularly type 14) produced disease. Streptococci of other groups produced no symptoms. No cases of nephritis or acute rheumatism occurred over the period of the investigation. None of the 12 children observed over 3 years were reinfected with organisms of the same type. Organisms of the same type of group A streptococci persisted in the throat for about 2–3 months.

2 of the laboratory workers carried non-typable group A strains at the beginning of the investigation, 5 acquired streptococci, 4 accompanied by sore throat but there was no epidemic among this group.

12 of the 35 old people were infected with group A streptococci, 2 with symptoms and an epidemic of Group G streptococci without illness lasted 1·5 years and involved 50% population. [The figures for this paper do not appear in the journal and must be obtained from the authors.] *M. Patricia Jevons*

LANCEFIELD, Rebecca C. **Persistence of Type-Specific Antibodies in Man following Infection with Group A Streptococci.** *J. Exper. Med.* 1959, Aug. 1, v. 110, No. 2, 271–92. [15 refs.]

Rebecca Lancefield has drawn on her extensive stock of Group A haemolytic streptococci, collected over more than 30 years, and on her continuing acquaintance with many of the patients from whom they were isolated, to determine the persistence of bactericidal antibodies in the serum. In most cases no antibiotic treatment had been given for the original infection. In 12 persons type-specific antibodies, determined by direct or indirect bactericidal tests [see this *Bulletin*, 1958, v. 33, 173] with the homologous streptococcus were demonstrated between 4 and 32 years after the infection; 13 other individuals with known infections 1 to 31 years previously had no antibodies. Antibodies to several types were present in some individuals. Persistence of antibody could not be related to the severity of the original infection. Mouse-protection tests were used to confirm the blood bactericidal tests in a few cases.

During the course of these studies it was found that the M antigen content of a streptococcal strain seemed to be measurable to some extent by its behaviour in fresh human blood: those with no M failed to grow, those with some M grew in the blood if the tubes were held stationary but not if they were rotated, while those with much M grew well even in rotated tubes. The strains rich in M needed a greater concentration of serum to produce a bactericidal effect in fresh blood than those with little M. This means that, in testing sera for bactericidal antibodies, it is important to use a strain with an appropriate M content.

R. E. O. Williams

BÖSZÖRMÉNYI, J., BOZSÓKY, S. & BARSY, G. **Data on the Significance of Standardization in determining O-Antistreptolysin Titre.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 2, 125–9. [13 refs.]

Antistreptolysin O (ASO) determinations were performed by two different Budapest laboratories on the

sera of 100 randomly selected patients. The same standard ASO was used in each laboratory but the other reagents and techniques were different. The corrected results, obtained by comparison with the standard, exhibited a statistically significant deviation between the two laboratories of approximately 10%. In a serological test using a 2-fold dilution series this is considered within the acceptable limit of error and the authors attribute the good agreement to the use of an ASO standard. *H. Gooder*

KRASNER, R. I. & YOUNG, Genevieve. **The Streptokinase-Plasminogen System. I. Its Effect on the Pathogenicity of Streptococci and other Organisms for Mice.** *J. Exper. Med.* 1959, Aug. 1, v. 110, No. 2, 245–58, 1 fig. [29 refs.]

The streptokinase-plasminogen system is shown to contribute to the pathogenicity of streptokinase (SK) positive streptococci for mice and to increase the virulence of other organisms including some which do not produce fibrinolysin.

Mice were infected intraperitoneally with suspensions of SK-producing Group A streptococci in saline; in SK and human plasma; and in plasma or SK alone. Varidase was used as the source of SK. There was an increase in mortality when organisms were suspended in SK and plasma or plasma alone but not in SK alone in 6/7 tests. Human plasminogen or serum was as effective as plasma, and rabbit plasma or plasminogen produced similar results in spite of the relative insusceptibility of rabbit fibrin to lysis. Since SK alone did not increase the mortality, it is suggested that these strains were producing the maximum effective amount of SK.

Cell suspensions of an SK-negative group D streptococcus in SK and plasma or plasminogen caused a higher mortality than suspensions in saline, plasma or SK alone. Similar results were obtained when an SK-variable strain of *Salmonella paratyphi A* was used, probably because insufficient fibrinolysin was produced early in the infection. Plasma alone increased the pathogenicity of an SK-negative coagulase-positive staphylococcus as effectively as in combination with SK. Plasminogen alone was ineffective. It is suggested that increased virulence of this organism in absence of SK was due to a coagulase activator in the plasma.

M. Patricia Jevons

HEDLUND, P. **Absorption Experiments with Acute Phase Protein in Human Serum.** *Acta Path. et Microb. Scandinavica.* 1959, v. 45, No. 3, 267–74.

" (1) Cross absorption experiments have been performed in order to study whether the substances present in acute phase serum and which can be demonstrated with C-reactive Protein Antiserum (CRPA) and the Löfström Capsular Swelling Reaction (CSR), are identical.

" (2) For the absorptions suspensions of pneumococci of types 1, 23B and 27, CRPA, C-polysaccharides of types 1, 23B and 27, suspensions of hemolytic streptococci type 1 Lancefield (Dochez strain), and bovine albumin were used.

" (3) Absorption of acute phase sera with suspensions of pneumococci of type 23B and 27 removed all CRPA-reacting substance.

" (4) The CRPA absorbed all the substance which gave a capsular swelling reaction with type 23B and 27.

" (5) Polysaccharides produced from type 1, 23B and 27 absorbed capsular swelling substance but not all the CRPA-reacting substance. This may depend upon acute phase protein consisting of two or more substances.

" (6) Hemolytic streptococcic strain type 1 (Dochez) and bovine albumin did not absorb acute phase protein."

LINDE, K. Über enteropathogene Darmstreptokokken. **[The Entero-Pathogenic Intestinal Streptococci]** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 5/6, 363–72. [21 refs.]

Investigation of faeces from victims of an outbreak of acute diarrhoea, affecting altogether 190 youths in a work camp, failed to reveal any pathogenic enterobacteria. Staphylococci were not sought. From some patients enterococci were isolated and 10 of these were put up for agglutination tests with sera taken from 15 patients 3 weeks after the illness. 1 strain was agglutinated at 1:800 or more by all sera, the others only at lower titres; none of 150 sera sent in for routine diagnostic serology had a titre of more than 1:200 for this strain. None of 5 volunteers who consumed a culture of the enterococcus had significant symptoms.

R. E. O. Williams

ODAKA, T. & WATANABE, T. **Transformation Reaction of Pneumococci in the Absence of Serum Factor.** [Correspondence.] *Nature.* 1959, Aug. 8, v. 184, Suppl. No. 7, 471–2, 1 fig.

ALDRIDGE, C., FELTON, Frances G., MUCHMORE, H. G. & RAMSEY, H. H. **A New Liquid Synthetic Medium for the Cultivation of Mycobacterium Species.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 267–8, 1 fig.

This medium, which is chemically defined, is applicable to many growth and nutritional studies, and being colourless is particularly suitable for spectrophotometric readings; it is, however, not recommended for diagnostic purposes.

It consists of KH_2PO_4 5·0 gm., NH_4Cl 5·0 gm., Mg citrate 1·0 gm., K_2SO_4 0·5 gm., ferric ammonium citrate 0·0025 gm., Tween 80 0·2 ml. and distilled water to 980 ml. After adjusting the *p*H to 6·8 the medium is sterilized by heat and 20 ml. of sterile 50% glucose is then added. Aeration by either occasional or constant shaking increases the yield of tubercle bacilli; growth is a little slower but by the 15th day it equals that in Dubos medium. *S. R. M. Bushby*

SULA, L. **Fibrin-Clot Culture Technique for Isolation of Tubercle Bacilli from Pleural Exudates.** *Amer. Rev. Respiratory Dis.* 1959, Sept., v. 80, No. 3, 438–40, 2 figs.

GALE, D. & LOCKHART, Elizabeth A. **The "Bluing" Phenomenon: a Source of Contamination in Cultures of Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1959, July, v. 80, No. 1, Pt. 1, 95–9.

This form of contamination which occurs with media containing malachite green was observed to be more common among cultures made from gastric washings than among those from sputa. The "bluing" is due to a decrease in *p*H and in this study the change was associated with the growth of 3 organisms; these were an alpha streptococcus, an enterococcus and a non-haemolytic staphylococcus.

Experiments showed that the enterococcus and the staphylococcus were resistant to 3 hours' alkali treatment and would grow on appropriate media despite the production of sufficient acid to produce a *p*H of 4·5 or less; the alpha-haemolytic streptococcus was killed by the alkali treatment.

The authors conclude that the "bluing" phenomenon in cultures is mainly due to enterococci and that the growth of the organism is inhibited for several days by the alkali treatment but growth occurs as soon as the acid, produced by its metabolism, is sufficient. The growth of 3 strains of tubercle bacilli were shown to be inhibited at *p*H 4·5, thus accounting for cultures which show this "bluing" always being negative for tubercle bacilli.

[See also this *Bulletin*, 1959, v. 34, 161.]

S. R. M. Bushby

FARMER, Pauline. **The Effect of Surface Moisture on Colonial Morphology of BCG.** *Tubercle.* 1959, Apr., v. 40, No. 2, 121–3, 4 figs.

The appearances of the colonies of sub-strains of BCG vary with the physical conditions. Strains normally growing as discrete smooth colonies have been shown to form serpentine, rough colonies when grown in the presence of excess surface moisture, and microscopic examination of such colonies, growing on nutrient agar containing 10% blood, show that the "cords" of bacilli are much tighter than in the smooth colonies.

The bacilli of the Moreau sub-strain consisted only of loose cords and this observation correlates with its reported low invasiveness in man, for in guineapigs smooth varieties are known to produce smaller local lesions than rough varieties. *S. R. M. Bushby*

MACKEPRANG, B. **Effect of Ultrasonics on Young and Old BCG Cultures, evaluated by Degree of Dispersion, Germinating Ability and Lag Time.** *Acta Path. et Microb. Scandinavica.* 1959, v. 45, No 4, 371–80, 2 figs. [15 refs.]

"Some biological aspects (degree of dispersion, germinating ability and lag-time) are examined in a young (3-day-old) and an old (5-week-old) BCG culture, before and after exposure to ultrasonics for 20 and 120 minutes at an intensity of 0·56 watt/cm².

"The lag times in Dubos fluid medium with Tween are calculated on the basis of the growth curves determined by photometry and the number of living bacteria per ml. immediately after inoculation of the medium.

"The experiment shows the following:

"(1) The old culture is considerably more finely dispersed than the young culture.

"(2) The old culture becomes dispersed more rapidly and more effectively by means of ultrasonics than the young culture.

"(3) The two cultures are equally sensitive to the bactericidal effect of ultrasonics.

"(4) In sub-cultures in Dubos fluid medium with Tween, the young culture continues to grow without lag time.

"(5) Sub-culture of the old culture on to the same medium shows a lag period of about 36 hours.

"(6) Exposure of the two cultures to ultrasonics for 20 and 120 minutes causes no change in the lag times.

"Brief mention is made of the presuppositions and sources of error in the method used for determination of the lag periods."

KATO, M., KUSUNOSE, M., MIKI, K., MATSUNAGA, K. & YAMAMURA, Y. **The Mechanism of the Toxicity of Cord Factor.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 240–48, 3 figs. [24 refs.]

The injection of 0·1 mgm. of purified cord factor intraperitoneally into mice lowers the succinic, malic, lactic and α-glycerophosphoric dehydrogenase activity of homogenates of the liver of the animals 6–72 hours after the injection, triphenyltetrazolium chloride (TTC) being used as the acceptor; no effects were, however, observed on the reduction of the TTC with citrate, glutamate or alanine. The minimum effective dose of the factor was shown to be 5 μgm. but there was no relationship between the dose and the reduction in enzyme activity. The factor had no effect on the enzyme when added *in vitro* to homogenates of normal liver, indicating that the factor does not directly inhibit the electron transfer from succinate to TTC.

Experiments with "antipiricrin" and cyanide indicated that the reduction of TTC is *via* the cytochrome system and experiments with homogenates of the livers of normal and cord-treated mice, in which the reduction of ferricyanide and oxygen consumption through methylene blue were measured, showed that the cord factor impairs in some way the enzymatic activity of succinic dehydrogenase but not that of the cytochrome-oxidase system.

The decreased activity of succinic and α-glycerophosphoric dehydrogenase of the liver were restored when the liver was homogenized with mitochondria-containing sucrose extracts of normal liver. *S. R. M. Bushby*

HOBBY, Gladys L., LENERT, Tulita F., STASKO, Irene & MAUSER, Marie. **Further Observations on the Biologic Activity of Crude Mycobacterial Cells.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 274–6, 3 figs.

These experiments are a continuation of those described in previous papers [this *Bulletin*, 1959, v. 34, 484 *bis*] in which phenolized and lyophilized virulent tubercle bacilli, grown *en masse*, were shown to be as effective in protecting animals against challenge with

living virulent tubercle bacilli as phenolized non-living BCG grown under the more conventional conditions.

The present experiments were made in mice vaccinated with lyophilized dead vaccines of virulent and avirulent strains of bovine and human tubercle bacilli and then challenged with the Vallée bovine strain, injected intravenously. The results suggest that dosage and mode of administration are more important than the vaccine strain, and they support the authors' previous contention that killed bacilli can produce as good protection as live BCG. *S. R. M. Bushby*

HOYT, A., THOMPSON, Millie A., MOORE, F. J. & SMITH, C. R. **Some Fractions of Tubercle Bacillus Wax and their Immunogenicity for Mice.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 216–22. [20 refs.]

The wax used in these experiments was that of Anderson and consists of the reprecipitated portion of a chloroform extract of tubercle bacilli previously extracted with ethanol-ether; as this wax still contained tubercle bacilli or bacillary fragments, the authors have previously considered them to be responsible for the immunizing property of the wax.

In these present experiments mice were vaccinated with 5 fractions of the wax and then challenged with H37Rv injected intravenously. The fractions were obtained by dissolving the wax in *n*-heptane and separated by differential centrifugation and drying. The wax and 4 of the fractions afforded definite protection, but the fifth fraction was inert. This inert fraction, which consisted of 30% of the wax, was the supernatant of the extract, centrifuged at 35,000 r.p.m. The possibility of the immunizing property of the other fractions being due to the presence of bacillary fragments was excluded by showing that the filtration through 300 mμ Millipore filters did not affect the immunizing properties of the fractions.

Details of solubility in heptane, octane and hexadecane are given for the fractions along with the melting points and nitrogen contents for some of them.

S. R. M. Bushby

PATTERSON, D. S. P. **The Chemical Composition of Weybridge PPD.** *Tubercle.* 1959, Apr., v. 40, No. 2, 71–81, 1 diagram. [26 refs.]

Since 1946 an adaptation of the Seibert method of extracting PPD has been used at Weybridge. The PPD produced there has been recognized as containing polysaccharides and nucleic acid but the fact that it was unusually stable to heat and to storage and that in the presence of tuberculous sera it fixed complement, suggested the presence of additional non-protein constituents.

An analysis of several preparations has shown that only 63% of the dried weight consists of protein and about 2% of polysaccharides; the remainder is composed of nucleic acid and lipid-soluble material. About 10% of the PPD consists of a lipid fraction that is readily soluble in water and methanol. This fraction, which neither fixes complement nor produces a significant intradermal reaction in tuberculous animals, has a low P and N content and is apparently made up of organic acids of intermediate molecular weight. A crude phosphatide fraction, present to the extent of about 0·2% of the PPD, is highly active in fixing complement and the author suggests that apart from acting as the complement-fixing hapten, it is also responsible for the greater stability of the Weybridge preparation by acting as a protective layer about the protein moiety.

S. R. M. Bushby

PEPYS, J., AUGUSTIN, R. & PATERSON, A. B. **Common Antigenic Components of Mycobacterial Extracts.** *Tubercle.* 1959, June, v. 40, No 3, 163–72, 1 fig. [22 refs.]

The agar-gel diffusion test was used for this investigation. The antisera were produced by injecting rabbits with H37Rv suspended in liquid paraffin in lanolin. The polysaccharide antigens of the culturable mycobacteria were from either culture filtrates or from liquid paraffin or methanol extracts of dried bacilli; the protein extracts were obtained by the methods used for the extraction of PPD. Saline extracts of the leprosy bacillus were obtained from human lepromin, after extraction with chloroform and ether, and similar extracts were made from rat lepromin tissue.

There were 3 common precipitating antigens found in the proteins from the human, bovine and avian tubercle bacilli, *Mycobacterium johnei, Myco. phlei* and human lepromin. 2 of these antigens were found in the culture filtrates and the polysaccharides extracted by the liquid paraffin. The rat lepromin contained 2 precipitating antigens in common with the PPD and polysaccharide preparations. The methanol extracts of *Myco. johnei* and *Myco. phlei* produced 2 precipitating lines in common with each other but apparently not with those of any of the other preparations, although inhibition tests with PPD and polysaccharide preparations showed that they were related.

Tests with proteolytic digests of some of the PPD preparations and carbohydrate-staining of the precipitation lines suggested that even with the protein antigens it was the polysaccharide component that was responsible for the precipitates. *S. R. M. Bushby*

BILLAUDELLE, H., INDIRA, M., MURTHY, P. S., RAMAKRISHNA, T., SIRSI, M. & WARFVINGE L. E. **Studies on Endotuberculin. II. Some Biochemical Properties of Endotuberculin from Human and Bovine Strains.** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, July, v. 118, No 1, 8–19, 8 figs. [18 refs.]

In an earlier paper [this *Bulletin,* 1958, v. 33, 271] the authors described the extraction of endotuberculin (ET) from tubercle bacilli by a freezing and thawing process. This tuberculin was highly active in intradermal tests but as it also produced skin hypersensitivity of the delayed type to OT it appeared to contain the same sensitizing agent as the whole bacillus. The authors have now started, in collaboration with WHO, a study of the possible value of ET as an immunizing agent. The extraction of ET was aided by the use of an apparatus in which the temperature automatically fluctuated 20

times between −56° and +40°C. The majority of the bacilli were reduced by this treatment to what appeared by electron microscopy as an amorphous mass containing ghost-like remnants of the bacilli. A few, however, still possessed the relatively normal structure of the polar-dense type, but none were acid-fast, and these are removed by Seitz filtration.

The previous investigation also indicated that ET is a lipopolysaccharide containing a small portion of protein or polypeptides. In the present study, paper chromatographic analysis permitted identification of 18 amino acids in the acid-hydrolysate, 14 of which were also present in the hydrolysate of the trichloracetic-acid-precipitate. Similar analysis of the free-sugars content revealed 6 benzidine-trichloracetic-acid-positive spots but only 2 of these were identified—1 was raffinose and the other was glucose. *S. R. M. Bushby*

TAKEYA, K.; MORI, R.; NAKASHIMA, Noritaka; KOIKE, M.; TODA T.; YUDA, Yasuma. **Light and Electron Microscope Studies of Mycobacterium-Mycobacteriophage Interactions. I. Light Microscope Studies** [TAKEYA, MORI, NAKASHIMA, KOIDE & TODA]. *J. Bacteriology*. 1959, Sept., v. 78, No. 3, 307–12, 6 figs. [17 refs.] **II. Electron Microscope Studies** [TAKEYA, KOIKE, MORI, YUDA & TODA]. *Ibid.*, 313–19, 19 figs. [10 refs.]

WHITE, A. & KNIGHT, V. **A Factor in Serum which prevents Propagation of D–29 Mycobacteriophage with Human Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1959, July, v. 80, No. 1, Pt. 1, 12–18, 2 figs.

The inhibitory effects of this factor were demonstrated by incubating for 48 hours the bacteriophage with tubercle bacilli suspended in Dubos medium without Tween 80, and then determining the increase in the phage particles by adding a volume of the suspension to plates seeded with the non-pathogenic mycobacterium, 607, and after 48 hours' incubation, counting the number of plaques.

When the propagating strain was H37Rv or H37Ra, propagation of the phage was shown to be inhibited by the presence of 10% or more serum, irrespective of whether it was from tuberculin-negative or -positive donors or from patients with tuberculosis, but the serum had no effect when the propagating strain was 607. The factor is destroyed by heating at 56°C. and experiments with serum fractions indicate that it is a gamma globulin. Other experiments, in which serum and the suspensions of the tubercle bacilli were centrifuged after incubation and the addition of phage and phage counts made on the supernatant fluid, showed that adsorption of the phage by the bacilli is not prevented by the serum and the authors therefore suggest that the inhibitory effect is on the bacillus rather than on the phage.

S. R. M. Bushby

WILLETT, Hilda P. **The Effect of Isoniazid on the Synthesis of Certain Amino Acids and Vitamins by** *Mycobacterium tuberculosis*. *Amer. Rev. Respiratory Dis.* 1959, Sept., v. 80, No. 3, 404–9 [15 refs.]

MAYER, R. L., EISMAN, P. C., GEFTIC, S. & KONOPKA, E. **The Antituberculosis and Antileprosy Activity of Disubstituted Thiocarbanilides. In Particular SU 1906.** *Internat. J. Leprosy*. Wash. 1959, Jan.–Mar., v. 27, No. 1, 8–25, 5 figs. [23 refs.]

On the basis of the taxonomic relationship between mycobacteria and fungi, numerous thioureas known to be potent fungicides were tested for activity against mycobacteria and many, especially certain disubstituted thiocarbanilides, showed high activity but this paper describes experiments with only 5 of them. *In vitro* and in guineapigs and mice, Su 1906 (4-butoxy-4′-dimethylaminodiphenylthiourea) showed the highest activity against the tubercle bacillus; it inhibits growth *in vitro* at concentrations of 1 μgm./ml., and 0·01% in the diet affords high protection in infected mice. In mice the activity was apparent even when the treatment was given for only 1 day or was delayed for 15 days after infection. In guineapigs, infected subcutaneously with H37Rv, Su 1906 gives protection comparable with that of isoniazid and markedly superior to that of PAS.

Su 1906 does not eliminate all the tubercle bacilli from guineapigs, and, although when treatment with 0·1% in the diet was stopped after 9 months, the extent of the disease 9 months later was not as extensive as that in the untreated animals, the protection under these conditions was less than that given by the same dose of isoniazid. In combination, sub-optimal doses of Su 1906 (0·005 and 0·01%) and isoniazid (0·005%) or streptomycin (1 mgm. s.c.) showed enhanced activity.

In vitro the presence of Su 1906 delayed the emergence of isoniazid and streptomycin resistant variants of H37Rv during serial sub-culturing in the drugs. Cross-resistance was noted to occur between Su 1906 and the thiosemicarbazones suggesting a common mode of action.

Su 1906 was active *in vitro* against 6 chromogenic bacteria isolated from cases of human tuberculosis. All these strains were resistant to streptomycin and PAS and 4 were resistant to isoniazid. The activity in infected mice showed little relationship to the *in vitro* activity but Su 1906 showed some activity against all 5 strains. In mice and rats infected with murine leprosy Su 1906 showed activity about one-half of that of isoniazid or DDS, but this effect was variable; in one experiment no activity was shown. [Very little detailed information of these latter experiments is given but the authors stress that their value for forecasting activity in leprosy is very doubtful.] *S. R. M. Bushby*

ILAND, C. N. & BARKER, Ruth M. **The Use of Skin Ulcer Measurements to estimate Immunity against Tuberculosis in the Guinea-Pig.** *Tubercle*. 1959, Aug., v. 40, No. 4, 235–44, 4 figs.

In an assessment of this method, guineapigs were vaccinated with BCG and challenged at various intervals with living vole bacilli injected intradermally. The diameters of the ulcers developing from the injection of the living bacilli were measured at weekly intervals for 8 weeks. The maximum size of the ulcers ranged from 5 to 10 mm. and this was reached in about 4 weeks.

The effects of the vaccination, which could be a reduction in both the size of the lesion and of the length of its duration, were evaluated by comparing the sum of the weekly sizes of the lesions of vaccinated animals with those of unvaccinated animals. The differences between the mean figures depended upon the intervals between vaccination and challenge, *e.g.* the mean of 5 unvaccinated animals was 70·9 mm. as compared with 35·5 mm. for 4 animals challenged 6 weeks after vaccination and 5·5 mm. for 2 animals challenged after 3 weeks.

Hypersensitivity to the vole bacillus was demonstrated by injecting dead bacilli, and in order to prevent this affecting the assessment of immunity, the size of this lesion was subtracted from that of the lesion produced by the living bacilli.

This method appears to be sensitive and precise, and significant results can be obtained with few animals; it therefore has advantages over mortality-rate determinations. *S. R. M. Bushby*

BERGQVIST, S. & PACKALÉN, T. **The Antibody Response of the Tuberculous Guineapig to Non-Tuberculous Antigens.** *Acta Path. et Microb. Scandinavica.* 1958, v. 43, No. 1, 73–9, 2 figs. [25 refs.]

"Tuberculous guineapigs respond to spontaneous staphylococcal infections with a stronger antistaphylolysin formation than non-tuberculous controls.

"Tuberculous guineapigs respond to α-staphylolysin and streptolysin-O immunization with higher antilysin titres than non-tuberculous controls.

"Possible mechanisms responsible for these immune phenomena are discussed."

URBANCIK, R. **Chemotherapy of Diseases caused by Atypical Mycobacteria. I.** *In vitro* **Response to a Number of Antimicrobial Agents in Blood Agar, 7H9 and Löwenstein Media.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 3, 306–13. [12 refs.]

"An investigation was undertaken to determine the in vitro response of atypical and other mycobacteria to a number of antimicrobial agents in blood agar, 7H9 and Löwenstein media. On the basis of the studies, and in order of their effectiveness, tetracycline, isoniazid, viomycin, streptomycin, thiocarbanilide, cycloserine, nebacetin, and perhaps PAS, spiramycin, ilotycin, bacitracin, aureomycin, chloramphenicol, sarcomycin, aristamid and gantrisin, either alone or in combination, appear to be of some value for the treatment of diseases caused by atypical photochromogenic strains of mycobacteria. Under the conditions of the experiment, terramycin, neomycin and novobiocin did not suppress the growth of atypical mycobacteria."

SELKON, J. B. & MITCHISON, D. A. **Atypical Mycobacteria and Drug-Resistant Tubercle Bacilli isolated during a Survey of Untreated Patients with Pulmonary Tuberculosis.** *Tubercle.* 1959, June, v. 40, No. 3, 141–54. [27 refs]

This extensive report is concerned with the 55 strains of mycobacteria, resistant to streptomycin, PAS or isoniazid, isolated from 1,081 newly diagnosed and untreated patients with positive culture during the National Survey for the incidence of resistant strains [FOX *et al.*, this *Bulletin*, 1957, v. 32, 995]. These strains were morphologically indistinguishable from tubercle bacilli when first isolated although 7 were later shown to be atypical mycobacteria; all except 1 of the cultures were shown to be pure and this exception was a mixture of bovine tubercle bacilli and an atypical mycobacterium.

22 of the strains were resistant only to streptomycin, and these were identified, as tubercle bacilli by their colonial morphology and their high virulence for guineapigs; the other strains were submitted to extensive biochemical and virulence tests.

The tubercle bacilli proved to be very consistent in their colonial appearances, in forming "cords", in not growing at 22°C., in being catalase-positive, unless the strain was resistant to 50 μgm. isoniazid per ml., in not reducing methylene blue, and in being neutral-red-positive; the bovine strains were, however, niacin-negative whereas the human strains were positive, and 1 bovine strain was arylsulphatase-positive.

The 7 atypical mycobacteria varied in morphology and in colonial appearance. 5 of them were photochromogens; these were virulent to mice, and were considered to be the cause of the pathological conditions of the patients. Another of these strains was a scotochromogen and it was avirulent to mice. (This was the strain isolated with a bovine bacillus.) The 7th strain was identified as an avian tubercle bacillus. Of the biochemical tests used for the identification of these bacilli, apearances on oleic-acid-albumin agar, resistance to thiosemicarbazones and a negative niacin test were the most valuable, and the authors suggest these tests along with the effects of exposure to light, and ability to produce catalase will enable many of the atypical strains to be identified with certainty.

S. R. M. Bushby

OKADA, S. **Electron Microscope Studies of the Murine Leprosy Bacillus.** *Internat. J. Leprosy.* Wash. 1958, Oct.–Dec., v. 26, No. 4, Pt. 1, 352–5.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 43.]

SCHNEWEIS, K. E. Zur Mikromorphologie glatter und rauher Enterobacteriaceen-Kulturen. [**On the Micro-Morphology of Smooth and Rough Variants of Enterobacteriaceae**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 176, Nos. 1/2, 71–83, 4 figs. on 2 pls. [14 refs.]

KAUFFMANN, F. **Supplement to the Kauffmann-White Scheme (I) & (II).** *Acta Path. et Microb. Scandinavica.* 1958, v. 43, No. 3, 247–53; 1959, v. 45, No. 4, 411–16.

i. "A supplement to the review '*Das Kauffmann-White Schema*' is given, containing some data and 71 new *Salmonella* types recognized during the year 1957."

ii. "A supplement to the review '*Das Kauffmann-White Schema*' is given, containing some data and 53 new *Salmonella species* recognized during the year 1958."

WILSON, Virginia R. & EDWARDS, P. R. **Five New Bacteriophage Types of *Salmonella typhi*.** *Pub. Health Lab.* 1959, May, v. 17, No. 3, 66–7.

This is merely a record of the establishment of 5 further phage types of *Salmonella typhi*. In each instance Vi phage II, type A, was adapted to a culture of *Salm. typhi* which was completely, or almost completely, resistant to the routine dilutions of the phage adaptations used in typing. E. S. ANDERSON, Head of the International Reference Laboratory for Enteric Phage Typing, London, has confirmed these findings and the types are designated as C_7, C_8, C_9, D_8 and F_3. It is to be noted that types C_9 and D_8 carry temperate or symbiotic phages active against *Salm. typhi* type A and *Salm. typhi* 901 O. [See also this *Bulletin*, 1957, v. 32, 185.] *H. J. Bensted*

PETROSYAN, E. A. & ZVENIGORODSKAYA, V. P. **A Study of the Antigens of the Enteric Organisms—I. Immunochemical Study of the Vi Antigen of Typhoid Bacilli.** *J. Microbiol., Epidemiol. & Immunobiol.* London, 1957, v. 28, Nos. 7/8, 1167–71. [Translated from Russian.]

"(1) Study of Vi antigens obtained in various ways from the typhoid strain Vi 1 Bhatnagar showed that they resemble each other in general chemical composition and have marked specificity and antigenic properties.

"(2) Results of study of the chemical nature of the Vi antigen indicate the presence of polysaccharide, protein and lipid components, which illustrates the complexity of its molecular structure."

PETROSYAN, E. A. & ZVENIGORODSKAYA, V. P. **A Study of the Vi Antigen of Organisms of the Enteric Group—II. An Immunochemical Study of the Vi Antigens of *Escherichia coli* and *Salmonella ballerup*.** *J. Microbiol., Epidemiol. & Immunobiol.* London, 1957, v. 28, Nos. 9/10, 1484–91. 1 fig. [Translated from Russian.]

The Vi antigens of organisms in the family of the Enterobacteriaceae, other than *Salmonella typhi*, have been extensively investigated by a number of workers in recent years either as pure immunological or immunochemical studies (see WEBSTER *et al.*, this *Bulletin*, 1953, v. 28, 215; LANDY and WEBSTER, *ibid.*, 216; FELIX, *ibid.*, 373. *J. Hygiene*, 1952, v. 50, 515, etc.). The experiments reported in this paper are of the same nature as those carried out by Landy and his colleagues and the results are of the same order. The protective effect of preparations containing Vi antigen, as measured in mice against a challenge with a virulent strain of *Salm. typhi*, is directly related to their Vi antigen content. The *Escherichia coli* strain 5396/38 is very rich in Vi antigen and has the highest immunizing activity. Most other workers have found the Bailerup strain to come next in order, but the present authors were unable to show any significant difference in Vi antigenicity between Ballerup and *Salm. typhi* Ty2 (Landy's results, taking the antigenicity of *Salm. typhi* Ty2 as unity, showed that the figure for the Ballerup strain was 5·5 and that of the *E. coli* strain 5396/38 was 12).

Although the present authors employed slightly different techniques for the preparation of the Vi extracts the investigation was virtually a repetition of work which is already familiar to those interested in this particular subject. *H. J. Bensted*

GINTSE, L. A. **The Significance of the Experimental Determination of the Toxicity of Typhoid and Paratyphoid Strains in the Assessment of their Immunological Activity.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 3/4, 521–6, 4 figs. [Translated from Russian.]

According to the instructions the author was expected to follow in selecting strains for typhoid-paratyphoid vaccine preparation the organisms should combine high virulence for mice, high immunogenic power and almost complete absence of toxicity when the killed organism was injected into mice. The substance of this paper is concerned with the demonstration of the unreality of these instructions and the author concludes, after examining 200 strains of typhoid-paratyphoid bacilli, that there is a direct relationship between toxicity, virulence and immunogenicity and that it is impossible to select strains for vaccine production that are at the same time highly virulent and immunogenic but of low toxicity. [While it may be reasonable to question the reality of any administrative instructions relating to scientific procedure, it cannot be said that the author's experiments were entirely convincing. In fully controlled experiments it would be surprising to find that 500 million killed typhoid or paratyphoid bacilli injected intraperitoneally into mice of 16–18 gm. regularly caused death. In the experience of the reviewer the dose needed would be at least 10 times this figure. The experiments described, however, do not include sufficient detailed information to enable any proper assessment to be made.] *H. J. Bensted*

GREENBERG, B. **Persistence of Bacteria in the Developmental Stages of the Housefly. I. Survival of Enteric Pathogens in the Normal and Aseptically Reared Host.** *Amer. J. Trop. Med. & Hyg.* 1959, July, v. 8, No. 4, 405–11, 6 figs. [11 refs.] **II. Quantitative Study of the Host-Contaminant Relationship in Flies breeding under Natural Conditions.** *Ibid.*, 412–16, 4 figs.

I. The culture medium used for the fly eggs was a proprietary substance called CSMA; it contained wheat bran 33%, alfalfa meal 26·7% and brewers' grain 40%. This was mixed with tap water for use in the proportion of 14 gm. CSMA to 30 ml. water and feeding dishes containing this medium were seeded with the fly eggs intended for culture. It was not a sterile medium,

but it was not deliberately contaminated at this stage. The egg cultures were returned to the fly cages which were kept at 36°C. When the maggots had reached the 3rd instar 5 ml. of a 24-hour broth culture of the test organism (*Salmonella typhi* Vi strain, *Salm. paratyphi B*, *Salm. enteritidis* or *Shigella flexneri* 2a) were pipetted into the medium. Specimens were withdrawn at various stages of development and, after suitable treatment, were examined for evidence of survival of the inoculated test organism. *Sh. flexneri* was recovered infrequently from the larvae but never from the adult fly, whereas a more resistant organism—*Salm. paratyphi B*—was recovered from both forms though more often from larvae. When, however, these experiments were repeated with CSMA which had been previously sterilized all the test organisms were routinely recovered from larvae and pupae of various ages. Pathogens were thus able to survive pupation and multiply in the absence of competition from the natural flora (*Proteus*, *Aerobacter* and *Escherichia*) and the elimination of the typhoid and Flexner organisms was probably due to the overgrowth of the other bacteria.

II. The bacterial content of the various developing forms whether bred on CSMA in the laboratory or under natural conditions is much the same for each stage. There is a progressive fall from mature maggots with a mean figure of 10^7 through the prepupal stage, pupation to emerging adults where the figure is 10^2–10^3 organisms per adult fly. Infection with a single species of pathogen under optimum conditions and multiple saprophytic flora infections exhibit a pattern of survival which is essentially the same in all cases. There is no evidence to show that the normally contaminating flora survive any better than pathogens in the gut of the developing fly.

[It will be recalled that in his *Flies in Relation to Disease* (1914, Cambridge University Press), GRAHAM-SMITH gave the current view that Morgan's bacillus and the paracolon bacilli survived through the metamorphosis to the adult stage but that typhoid bacilli rarely survived. This interesting paper offers evidence to show that any failure on the part of typhoid bacilli, or the other pathogenic bacteria tested, to survive is due to their failure in the competition against the other bacteria and is not related directly to the developing fly itself.] *H. J. Bensted*

MIYAKE, T. **Fertility Factor in** *Salmonella typhimurium*. [Correspondence.] *Nature*. 1959, Aug. 22, v. 184, Suppl. No. 9, 657–8.

KERRIDGE, D. **Synthesis of Flagella by Amino Acid-Requiring Mutants of** *Salmonella typhimurium*. *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 168–79, 1 fig. [18 refs.]

CHRISTIAN, J. H. B. **The Effects of Washing Treatments on the Composition of** *Salmonella oranienburg*. *Australian J. Biol. Sci.* 1958, Nov., v. 11, No. 4, 538–47, 5 figs.

The motile salmonella organisms form a homogeneous group in regard to their water relations [this *Bulletin*, 1954, v. 29, 663, 666; 1955, v. 30, 906; 1956, v. 31, (568)] and it may be assumed that the results obtained from a study of the effects of washing treatments of *Salmonella oranienburg* would apply to the whole group and probably also to the family Enterobacteriaceae. Cells of *Salm. oranienburg* grown in liquid media of water activity (a_w) 0·993 were washed in water and in solutions of sucrose, glycerol, NaCl,KCl,NH_4Cl and $MgSO_4$ at a range of a_w. At *p*H 7·5 cells retained most sodium after washing in water, while the retention of potassium and ultraviolet-absorbing compounds was greatest after washing in isotonic sucrose and electrolyte solutions. Changes in the *p*H of the washing solutions significantly affected the retention of cell constituents and a *p*H close to 7 is recommended. In choosing the solution to wash the bacterial cells it may be detrimental to use a solution the concentration of which is hypotonic to the culture medium. Sucrose would appear to be preferable to electrolytes. If electrolytes are used, those with cations of smaller hydrated ionic radii (potassium and ammonium) should be avoided.

When cells were washed in solutions of a_w from 1·000 to 0·990 the contents of potassium and ultraviolet-absorbing compounds in the cells was a function of a_w while the sodium content was largely dependent on the nature of the washing solute. *H. J. Bensted*

COLLARD, P. & SEN, R. **Salmonellae isolated at Ibadan. Second Report: Strains isolated during 1957.** *West African Med. J.* 1959, June, v. 8 (n.s.), No. 3, 114–16. [10 refs.]

"During 1957, thirty-one species of Salmonellae were isolated which have not previously been reported from Nigeria. Among these, sixteen were new types, twelve of which were from man and four were from animal sources."

New Types

Salm. agbeni	13, 23, 36 : gm
„ *amunigun*	16 : a : 1, 6
„ *ank*	28 : k : enz_{15}
„ *bukuru*	6, 8 : b : lw
„ *ekotedo*	9, 46 : z_4 : z_{23}
„ *gwoza*	1, 3, 19 : a : enz_{15}
„ *ititaba*	9, 46 : c : z_6
„ *jericho*	4, 12, 27 : c : enz_{15}
„ *jos*	1, 4, 12, 27 : y : enz_{15}
„ *lishabi*	9, 12 : z_{10} : 1, 7
„ *mapo*	6, 8 : z_{10} : 1, 5
„ *mokola*	3, 10 : y : 1, 7
„ *offa*	41 : z_{38}
„ *okerara*	3, 10 : z_1 : 1, 2
„ *onireke*	3, 10 : d : 1, 7
„ *oritamerin*	6, 7 : i : 1, 5

HUET, M. Une nouvelle *Salmonella* pathogène pour l'homme: Salmonella Tunis. A propos de 50 observations. [**A New** *Salmonella* **Pathogenic for Man: Salmonella Tunis**] *Bull. Acad. Nat. Méd.* 1958, v. 142, Nos. 27/28, 729–32.

Salmonella Tunis was first isolated in Tunis in 1956 (LE MINOR *et al.*, *Ann. Inst. Pasteur*, 1956, v. 91, 936).

It has the antigenic formula: 1, 13, 23; y; z_6. Unlike many new salmonella serotypes Salm. Tunis appears to have established itself almost at once as an important epidemiological type and within two years of its first isolation it has supplanted, with the exception of the enteric group of organisms, all the other salmonellae. Previously Salm. Brandenburg had been the dominant salmonella type in Tunis but several other serotypes could, at the same time, be isolated from the community. Now Salmonella Tunis is the only type found in faecal cultures from cases of gastroenteritis and it appears to be responsible for some very severe clinical conditions in young people. 3 case histories are given. *H. J. Bensted*

ALIN, K., HEILBORN, V. & HEINERTZ, N. O. **A New *Salmonella* Type. Salmonella Goeteborg (9,12: c:1,5).** *Acta Path. et Microb. Scandinavica.* 1959, v. 46, No. 1, 72.

"The authors describe a new Salmonella type *S. goeteborg* with the antigenic formula 9,12 : c : 1,5. The strain was isolated from a woman with fever."

SANDBU, P. & BÖVRE, K. **A New *Salmonella* Type: Salmonella Adamstua=11:e,h:1,6.** *Acta Path. et Microb. Scandinavica.* 1959, v. 45, No. 3, 319.

"The authors describe a new *Salmonella* type, *S. adamstua* = 11 : e,h : 1,6, isolated from a tortoise in Oslo."

HEILBORN, V., EKSTAM, M. & KARLSSON, K. A. **A New *Salmonella* Type (S. Kristianstad).** *Acta Path. et Microb. Scandinavica.* 1959, v. 45, No. 3, 320.

"A new *Salmonella* type *S. kristianstad* with the antigenic formula 3,10 : z_{10} : e,n,z_{15} is described. The strain was isolated from meat-flour produced in Sweden."

KAUDEWITZ, F. **Production of Bacterial Mutants with Nitrous Acid.** [Correspondence.] *Nature.* 1959, June 27, v. 183, 1829–30, 2 figs.

Nitrous acid has already been shown by MUNDRY and GIERER (*Nature*, 1958, v. 182, 1457) to produce mutants of tobacco mosaic virus by chemically altering its ribonucleic acid. In the present paper Kaudewitz studies the mutagenic effect of nitrous acid on *Escherichia coli* and *Salmonella typhi-murium*, the genetic substance of which is deoxyribonucleic acid.

The inactivating power of nitrous acid on bacterial cells is more marked on the actively dividing cell than when it is in the resting stage. The synthetic abilities of wild-type *E. coli* cells, which had survived nitrous acid treatment, were tested by replica-plating the colonies on minimal medium (containing only glucose and inorganic salts). This medium supported growth of the wild-type strain, but inhibited the multiplication of cells which had mutated to auxotrophy. With this technique it was found that nitrous acid was a powerful mutagen: with an inactivation rate of 10^{-5} about 4% of the surviving cells were auxotrophic mutants, and there was evidence to show that the mutational effect of nitrous acid on the living cell was direct—due to the conversion of adenine, guanine and cytosine in the deoxyribonucleic acid to hypoxanthine, xanthine and uracil. Further evidence indicated that in order to obtain a mutation detectable under the conditions of the experiment, the nitrous acid must affect both strands of the double-helix of the deoxyribonucleic acid molecule. *H. J. Bensted*

GOL'DFARB, D. M. & YERSHOV, F. I. **Modification of the Phage Titre Increase Test for the Investigation of Materials containing Free Phage.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 12, 1904–8. [Translated from Russian.]

The presence of certain bacteria in specimens such as river water or sewage has been detected by incubating the specimen in broth with phage specific for the organism in question, and then titrating the phage. A rise in titre of the phage indicates the presence of the organism. The authors point out that the test is invalidated if the specimen contains free phage, as it may well do. They have overcome this difficulty by mixing the specimen with a substance which kills phage without affecting the viability of bacteria, and which can be removed before the test phage is added.

In model experiments, it was found that 100–400 μgm. per ml. of dimesol 14 (= hydrochloride of 2-bis (2-chloroethyl) methylbenzimidazole) shaken for 30 min. at room temperature with 3×10^8 particles per ml. of a typing phage specific for *Shigella flexneri* 6 (Newcastle) inactivated 99% of the phage without killing the bacteria. The compound, which is insoluble, was completely removed by low speed centrifugation. Its effect on phage is thought to arise from its affinity for DNA. The test thus modified was found to be satisfactory.

[This is a clearly presented paper and gives quantitative details of the experiments done and their controls.] *Janice Taverne*

MILIAYEVA, E. N. **Determination of the Degree of Infection of Objects of Everyday Use with *Shigella* by means of the Titre Increase Reaction.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No 12, 1908–12. [Translated from Russian.]

This paper gives no information about the titre increase reaction [see GOL'DFARB and YERSHOV, above] beyond the fact that it is related to the reaction between a shigella phage and very low concentrations of viable shigella organisms. Various surfaces of inanimate objects were infected with cultures of shigellae in different concentrations and these surfaces were examined at increasingly long intervals from the date of inoculation. Unless the inoculum consisted of a concentrated suspension of shigella organisms the usual bacteriological procedures failed to demonstrate viable organisms after the first day whereas the phage titre increase reaction might continue to be positive up to the 10th day. While it can be assumed that the author

is putting forward a method for the determination of the infectivity of inanimate objects contaminated by shigella organisms which is superior to the usual cultural methods employed by bacteriologists, it is not possible to compare the results with those obtained by other workers in this field in the absence of detailed information about this phage titre increase reaction. It should be stated, however, that a reference to a Russian Conference is quoted. *H. J. Bensted*

EWING, W. H., REAVIS, R. W. & DAVIS, Betty R. **Provisional *Shigella* Serotypes.** *Canadian J. Microbiol.* Ottawa. 1958, Apr., v. 4, No. 2, 89–107. [31 refs.]

It will be recalled that in 1950, at the Rio de Janeiro Congress of the International Association of Microbiologists [this *Bulletin*, 1952, v. 27, 781; 1954, v. 29, 766], the Shigella Commission made certain recommendations relating to the nomenclature and definition of organisms that could be accepted as members of the *Shigella* group of dysentery bacilli. The Commission also recommended that the classification of the members of the group should follow the scheme proposed by EWING [*ibid.*, 1950, v. 25, 66], which as far as the mannite-fermenting bacilli were concerned stemmed from BOYD's classical work, the final report of which was published in 1940 [*ibid.*, 1940, v. 15, 576].

The Commission themselves had accepted for Subgroup A—the non-mannite-fermenters—7 valid types (*Shigella dysenteriae* Types 1–7). For subgroup B, comprising the mannite-fermenters with a distinct type antigen plus a complex group antigen, there were the distinct 6 serotypes together with the various subtypes, and these were to be known as *Sh. flexneri* (1–6 plus the subtypes). The subgroup C comprised the mannite-fermenting organisms of the group which had a distinctive type antigen, but no characteristic group-antigen complex that would have relegated it to the subgroup *Sh. flexneri*. This subgroup—*Sh. boydii*—comprised 11 acceptable serotypes. Subgroup D accommodated *Sh. sonnei*. There were a number of other so-called provisional serotypes which the Commission did not, at that time, accept as valid types but recommended they should be further investigated and considered for possible inclusion in the group at a later date depending on the additional information which might become available.

Since then the International Shigella Centres, in Atlanta, U.S.A., and London, England, have had opportunities of examining further strains of most of these provisional serotypes. These Centres receive a large number of shigella-like organisms for investigation and, in addition to the 7 serotypes set aside for re-investigation, there were 3 new provisional types included in the study together with the routine submissions.

The present report comes from the Centre in Atlanta, but it includes information from the Centre in London, and this now suggests that the previously described provisional serotypes 58 and 2050–52 should be added to subgroup A and named *Sh. dysenteriae* 9 & 10 respectively. In addition, provisional serotypes 123, 425, 2770–51 and 703 could be taken into subgroup C and named *Sh. boydii* 12, *Sh. boydii* 13, *Sh. boydii* 14 and *Sh. boydii* 15, respectively. Further it is suggested that certain other provisional serotypes should remain *sub judice*, pending additional information, and yet others be rejected as unacceptable to the group.

[In considering the exacting microbiological studies of the International Shigella Centres in Atlanta and London and the value of such an organization within WHO, particularly the outstanding work of Ewing, it is of some importance to relate these almost entirely laboratory studies to the world problem of bacillary dysentery as we see it to-day. 50 years ago bacteriologists were able to demonstrate that the most important organisms responsible for bacillary dysentery were what we now know as *Sh. dysenteriae* 1, *Sh. flexneri* and *Sh. sonnei*. The remarkable disappearance, or rather reduced incidence, of Shiga dysentery, even in the U.S.S.R. where it was for so long such a serious problem, can only be related to the general improvement in public and personal hygiene in those areas. Against this there has been the even more remarkable increase in the incidence of Sonne dysentery in all countries where the introduction of nurseries and child welfare clinics have been a prominent feature of their social programme. Excluding Sonne dysentery, *Sh. flexneri* would appear to be the most important cause of bacillary dysentery in Europe where Type 2a is generally the common type. In mental hospitals, however, *Sh. flexneri* 3 which, ever since type identification has been possible, has been, and continues to be—at least in the United Kingdom—almost the sole cause of dysentery in these institutions.

It is not suggested that the organisms described in the present report have any great epidemiological importance; they have been rarely encountered and have so far not been associated with any serious outbreak of clinical dysentery. Nevertheless their position has not been lightly established; it is only after long and careful consideration that the serotypes in question have been accepted by the authors as organisms which can be responsible for outbreaks of bacillary dysentery.]

H. J. Bensted

MULCYZK, Marian. Nowy ciepłochwiejny antygen pałeczek *S. flexneri* 3. [**A New Thermolabile Antigen of *S. flexneri* 3 Strains**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 2, 289–302. [20 refs.]

The English summary appended to the paper is as follows:—

"The strains isolated from patients with dysentery, referred to as serological variants of *S. flexneri* 3 with the antigenic formula III: 3, 4, 6 were found to contain a new thermolabile antigen, absent in all *S. flexneri* types and subtypes. The agglutinating properties of this antigen as well as its agglutinin binding capacity are fully destroyed after 2 hours' boiling at 100°C and after 20 hours' contact with N HCl. Its stimulating effect on the production of antibodies was also destroyed by 2 hours' boiling, whereas it was only attenuated by the treatment with N HCl. This antigen differs serologically and physicochemically from the

hitherto described thermolabile antigens of *Enterobacteriaceae*. In view of the physicochemical properties of this antigen, comparable to those of antigens α, β, γ and δ it has been termed antigen ϵ. The antigen ϵ exerts no inhibitory effect on the agglutination of living microorganisms in anti-O sera."

BAZILEVSKAIA, L. S., EL'KIN, S. B. & CHEBOTAREVICH, M. F. **The Production of Complete Antigen Preparations of Low Toxicity from *Shigella sonnei* —II.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1633–6. [Translated from Russian.]

A Boivin type of extract of *Shigella sonnei* was prepared and this antigen was hydrolysed and its antigenic properties and chemical structure studied. Chemically it differed significantly from *Sh. flexneri*. The Sonne antigen was richer in nitrogen and the amount of reducing substances left after hydrolysis with HCl was much less than in the Flexner antigen. The toxicity of both organisms was much reduced by hydrolysing for 50 minutes with 7·5 N acetic acid.

The antigenic properties were studied by hyperimmunizing horses with intravenous injections of the hydrolysed antigens and using the sera for agglutinin and precipitin tests and also for protection tests in mice. It was considered that the hydrolysed antigens of *Sh. sonnei*, in spite of their greatly reduced toxicity, retained adequate antigenic and immunogenic properties.

H. J. Bensted

COETZEE, J. N. **A Comparison of Various Methods of estimating Mutation Rates for the System Phase-I to Phase-II** *Shigella sonnei*. *South African J. Lab. & Clin. Med.* 1959, June, v. 5, No. 2, 103–12, 2 figs. [15 refs.]

"Various methods of estimating the mutation rate of phase-I to phase-II *Shigella sonnei* are examined, and it is concluded that the long-term method of continuous culture yields the only reliable estimate of the high rate of mutation involved."

[For Part I, see this *Bulletin*, 1959, v. 34, 1166.]

TROITSKY, V. L. **Experimental Research on Immunity to Dysentery.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 3, 257–65. [11 refs.]

Flexner dysentery was common as a natural infection among a herd of monkeys at a particular research station in the U.S.S.R., an observation which is by no means unique. It was found that such monkeys after recovery could withstand very large challenge doses of Flexner bacilli without showing any clinical sign of disease but they were susceptible to infection with cultures of *Shigella sonnei*. Monkeys which were carriers of Flexner bacilli after a natural infection or during the latent period of chronic would relapse after a challenge of 30×10^9 Flexner bacilli. In animals that recovered completely and ceased to excrete the infecting organism the specific post-infection immunity was relatively of short duration. This period of immunity could be significantly lengthened by repeatedly reinfecting such animals.

Immunization with killed vaccines was found have some effect in mitigating the course of the infection in monkeys so long as a series of doses with suitable intervals was given, but in monkeys continuing to excrete the organism after the original infection there was always a danger of the vaccine initiating a relapse. In such cases the author recommends prompt chemotherapeutic measures so that immunization could continue.

H. J. Bensted

BARBER, Cella, ISTRATI, Maria, SORU, Eugenia, GOREA, A. & ISTRATI, G. Vaccination anti-dysentérique. IV. Quelques propriétés chimiques et biologiques de dix différents extraits d'une souche de *Shigella flexneri* Type 2a. **[Antidysenteric Vaccination. IV. Some Chemical and Biological Properties of 10 Different Extracts from a Strain of *Sh. flexneri* Type 2a.]** *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Mar., v. 18, No. 1, 123–31. [22 refs.]

Previous studies by these authors on immunization against bacillary dysentery were reported in this *Bulletin* [GOREA *et al.*, 1959, v. 34, 927]. Owing to the severe reactions that frequently follow the administration of ordinary bacillary vaccines, which must be given in large doses if specific immunity is to be attained, the authors examined the antigenicity of a number of different extracts of *Shigella flexneri* 2a. The various extracts included distilled water, disodium phosphate, urea, ethylene-glycol, diethylene-glycol, glycerol, pyridine, phenol and hydrochloric acid as the extracting agent. When examined from the point of view of ratio between toxic and immunizing dose it was found that the ethylene-glycol, the pyridine and the hydrochloric acid extracts, in that order, gave the best results. As immunizing agents, although most of the extracts were superior to the trichloracetic acid extract of the Boivin type, not one of them proved to be superior to the ordinary bacillary vaccine—the suspension of the whole bacterial cells of *Sh. flexneri* 2a.

H. J. Bensted

WEINBACH, R., ISTRATI, G. & GOREA, A., with the technical collaboration of Ileana MĂLDĂRESCO. Vaccination anti-dysentérique. V. Établ'issement de la zone optime de *p*H pour l'adsorption de cinq extraits de *Sh. flexneri* 2a, sur support minéral, à l'aide de la méthode d'inhibition de l'hémagglutination indirecte. **[Antidysenteric Vaccination. V. The Zone of Optimal *p*H for the Adsorption of 5 Extracts of *Sh. flexneri* 2a on Minerals as established by the Method of Indirect Haemagglutination Inhibition]** *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Mar., v. 18, No. 1, 133–41. [20 refs.]

This paper describes the preparation of Flexner antigens by the adsorption of some of the more promising extracts described in the previous paper (see above) on to aluminium hydroxide or aluminium phosphate with the *p*H adjusted over the range 5–9 and employing the indirect haemagglutination-inhibition test to establish the degree of adsorption. The results were compared with the toxicity determinations carried

out on the supernatants of the various adsorbed antigens. Although there was a tendency at *p*H below 6·0 for non-specific haemagglutination to occur it was generally possible to calculate the percentage adsorption of the antigens. With the aluminium hydroxide the adsorption was complete in each case and was quite independent of the *p*H, whereas adsorption on the aluminium phosphate depended both on the *p*H and the particular antigen preparation. The authors consider that the high sensitivity of the indirect haemagglutination inhibition test offers a valuable method for determining the amounts of antigen extracted by different means from the Gram-negative bacilli.

H. J. Bensted

GELDREICH, E. E., CLARK, H. F., KABLER, P. W., HUFF, C. B. & BORDNER, R. H. **The Coliform Group. II. Reactions in EC Medium at 45°C.** *Applied Microbiol.* Baltimore. 1958, Sept., v. 6, No. 5, 347–8. [12 refs.]

Prompted by the suggestions of several workers that *Escherichia coli* was a more accurate indicator of faecal contamination than the more inclusive "coliform group" the present authors decided to examine a representative number of strains of twelve IMViC types, including *E. coli* I and II and to determine the percentage of each type that grew, with the production of gas, in EC medium when incubated at 45°C. [EC medium, introduced by HAJNA & PERRY (this *Bulletin*, 1943, v. 18, 943), is a buffered tryptose-lactose-bile-salt medium in which *E. coli* I grows and produces gas within 24 hours at 45°C.]

Each of the 5794 coliform cultures examined was tested for indole production, the methyl red reaction, acetyl methyl carbinol production and the EC reaction (gas in any amount after 24 hours at 45°C. was regarded as positive).

Of 1358 cultures from faecal sources, 1184 were classified as *E. coli* I, and 92·7% of them gave positive reactions in the EC test, whereas of 174 cultures classified as *E. coli* II only 21·8% produced gas in the EC medium at 45°C. With the remaining 4436 cultures from non-faecal sources, belonging to the other ten IMViC types, 7·8% gave positive EC reactions. There were, however, $^{61}/_{79}$ cultures with IMViC reactions: ++−−, that grew in EC media at 45°C. with gas formation. The authors feel that a further study of this group is indicated in order to determine whether or not these organisms have a faecal origin.

While the results reported here appear to be satisfactory it is not possible to assess the value of the EC medium in relation to other well tried media without controlled comparative trials.

[For Part I, see this *Bulletin*, 1958, v. 33, 494.]

H. J. Bensted

TAWIL, G. S. & EL KHOLY, S. **Serological Types of *Escherichia coli* in Association with Infantile Gastroenteritis.** *J. Bacteriology.* 1959, July, v. 78, No. 1, 13–17.

During an investigation of an outbreak of infant gastro-enteritis in a hospital in Egypt, 126 strains of *Escherichia coli* were isolated from 32 infants. All these strains were found to belong to O group 20 and to possess a K antigen of the B type. This B antigen was investigated by cross-absorption techniques and was found to have 5 components occurring in varying amounts from strain to strain. The flagellar antigens were not investigated, but 2 of the strains were found later to possess the antigen H34. *John S. Stevenson*

JELJASZEWICZ, J. & WŁODARCZAK, Krystyna. Wrażliwość *Escherichia coli* na niektóre antybiotyki, sulfonamidy i furadantyne. [**Sensitivity of *Escherichia coli* to some Antibiotics, Sulphonamides and Furadantine**] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 2, 113–18. [26 refs.]

The English summary appended to the paper is as follows:—

"Sensitivity of 100 Escherichia coli strains was investigated in reference to the action of penicillin, streptomycin, chloramphenicol, cholorotetracycline, oxytetracycline, erythromycin, bacitracin, neomycin, nebacetin (bacitracin + neomycin), furadantine, sulphathiazole and sulphamethylthiodazole. Penicillin, erythromycin, bacitracin, sulphamethylthiodazole and sulphathiazole presented a very weak action (100, 96, 97, 70 and 92% of resistant strains). A large number of strains was sensitive to the action of chloramphenicol, streptomycin and both tetracyclines but the majority of strains was found among the average sensitive ones (83, 80, 87 and 86% of strains). The strongest action was shown by neomycin, nebacetin and furadantine (100% of sensitive strains).

"The stronger action of these three drugs is particularly well seen during the observation of the average inhibition zones. The combination of bacitracin with neomycin possesses synergistic action. The tablet method employed for estimations by means of tablets made by Roskilde Medical Company, Roskilde, Denmark —is simple in performance and as to the accuracy of estimations it does not completely concede to the disc method."

LISOWSKI, J. WIECZOREK, Z. & KANTOCH, M. **Phagocytosis of *Escherichia coli* Protoplasts.** [Correspondence.] *Nature.* 1959, June 27, v. 183, 1828.

The phagocytosis of normal forms of *Escherichia coli* B and *E. coli* B protoplasts (produced by penicillin) were compared by estimating the phagocytic index (the average number of bacterial cells found in each leucocyte) after incubation for 20 minutes with normal fresh and inactivated serum both undiluted and diluted 1–10.

It was found that the indices obtained with suspensions of protoplasts were significantly lower than those obtained with the normal bacterial cells. When, however, reversion of the protoplasts to the mother cells was allowed to occur it was found that the phagocytic index returned to values of the same order as with the mother cells.

Protoplasts began to revert in broth at 37°C. After 6 hours' incubation, when both normal vegetative and protoplastic forms were present, the phagocytic index

was approximately the same as that found with normal cells. Further incubation up to 24 hours, when all cells had the typical vegetative form, did not significantly alter the index. *H. J. Bensted*

De Witt, C. W. & Rowe, J. A. ***N*,O-Diacetylneuraminic Acid and *N*-Acetylneuraminic Acid in** *Escherichia coli.* [Correspondence.] *Nature.* 1959, Aug. 1, v. 184, Suppl. No. 6, 381–2, 1 fig. [17 refs.]

Hedegaard, J., Maspero-Segre, Silvia, Nguyen-Van-Thoai & Roche, J. Influence de l'histidine et de ses métabolites sur la biosynthèse des purines par *Escherichia coli* B. IV. Action sur des cultures inhibées par l'azasérine. [**Influence of Histidine and its Metabolites on the Biosynthesis of Purines by** *Escherichia coli* **B. IV. Action on Cultures Inhibited by Azaserin**] *C.R. Soc. Biol.* 1959, v. 153, No. 5, 767–71, 3 figs. [24 refs.]

Love, S. H. & Levenberg, B. **Formation of 5-Aminoimidazole Riboside by** *Escherichia coli*: **Evidence for its Structure and Metabolic Relationship to the Purines.** *Biochim. et Biophys. Acta.* 1959, Oct., v. 35, No. 2, 367–73, 3 figs. [11 refs.]

Love, S. H. & Boyles, P. D. **Studies on the Synthesis of 5-Amino-4-Imidazolecarboxamide Ribotide by Cell-Free Extracts of** *Escherichia coli.* *Biochim. et Biophys. Acta.* 1959, Oct., v. 35, No. 2, 374–80, 4 figs. [21 refs.]

Wood, R. C. & Hitchings, G. H. **Effect of Pyrimethamine on Folic Acid Metabolism in** *Streptococcus faecalis* **and** *Escherichia coli.* *J. Biol. Chem.* 1959, Sept., v. 234, No. 9, 2377–80, 1 fig. [18 refs.]

Bessman, M. J. **Deoxyribonucleotide Kinases in Normal and Virus-Infected** *Escherichia coli.* *J. Biol. Chem.* 1959, Oct., v. 234, No. 10, 2735–40, 6 figs. [22 refs.]

Mandel, P., Sensenbrenner, M., De Gregorio, P. & Bader, A. M. **Distribution of Nucleic Acids among Different Stable *L* Forms of** *Proteus P* **18.** [Correspondence.] *Nature.* 1959, Aug. 15, v. 184, Suppl. No. 8, 566. [10 refs.]

Henriksen, S. D.; Eriksen, J. **Immunochemical Studies on some Serological Cross-Reactions in the** *Klebsiella* **Group. 1. A Quantitative Study of the Cross-Reactions between** *Klebsiella* **Types A (1), E (5) and AE** [Henriksen & Eriksen]. *Acta Path. et Microb. Scandinavica.* 1959, v. 45, No. 4, 381–6, 2 figs. [11 refs.] **2. Chemical Composition of the Capsular Polysaccharides** [Eriksen & Henriksen]. *Ibid.*, 387–91. [10 refs.]

Duguid, J. P. **Fimbriae and Adhesive Properties in** *Klebsiella* **Strains.** *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 271–86, 10 figs. on 4 pls. [18 refs.]

Krcméry, V. **A Rapid Biochemical Method for the Differentiation of** *Brucella suis.* **Peroxidase Activity of** *Brucella.* *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 3, 314–16.

"A rapid and easy biochemical method for identifying the strains of *brucella suis* on the basis of the peroxidase reaction is described. Briefly, 0·25 ml. of 0·5% pyrogallol and 0·25 ml. of 30% H_2O_2 is added to one ml. of suspension of brucella. The positive reaction shows itself by rapid darkening of the whole mixture and of its strong effervescence, and is quite specific for *brucella suis.*

"We did not find any strain of any other type of brucella which reacted in a similar way.

"The correlation of peroxidase and catalase activities in brucella is briefly discussed."

Khudanov, L. E., Shkurko, E. D. & Mikhno, V. S. **The Serological Relationship between** *Vibrio comma* **and** *Brucella.* *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 12, 1974–5. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 34.]

Dodin, A. & Brygoo, E. R. Étude quantitative de l'utilisation des sucres par *Pasteurella pestis* souche E. V. en suspension non proliférante. I. Le rhamnose. [**Quantitative Study of Glucide Uptake by** *Pasteurella pestis* **EV Strain, in Non-Proliferating Suspensions. I. Rhamnose**] *Ann. Inst. Pasteur.* 1959, Aug., v. 97, No. 2, 245–7, 1 chart.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 31.]

Ephrati-Elizur, Erela & Zamenhof, S. **Incorporation of 5-Bromouracil into transforming Principle of** *Bacillus subtilis* **and its Biological Effects.** [Correspondence.] *Nature.* 1959, Aug. 8, v. 184, Suppl. No. 7, 472–3, 1 fig.

Sheinin, Rose. **The Localization of the Cell-Bound Penicillinase of** *Bacillus cereus* **in Protoplasts.** *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 124–34, 3 text figs. & 3 figs. on pl. [33 refs.]

Scheibel, I. & Lennert-Petersen, O. **Effect of Antibiotics on Germinating Spores of** *Cl. tetani in Vitro* **and** *in Vivo.* *Acta Path. et Microb. Scandinavica.* 1958, v. 44, No. 2, 222–38, 6 figs. [29 refs.]

"The effect of different antibiotics *in vitro* on germinating spores of Cl. tetani Tulloch No. 3 has been investigated.

"It was found that all the antibiotics examined except polymyxin-B were bactericidal to varying degrees, the most effective being bacitracin, penicillin, oxytetracycline and tetracycline.

"The toxigenicity of the cells was not impaired by prolonged contact with growth inhibitory concentrations of antibiotics.

"There was no effect whatsoever on resting spores.

"It was shown by direct microscopy of slide cultures that the acquisition by the spores of antibiotic sensitivity occurs late in phase 1 before any signs of outgrowth are visible.

"Oxytetracycline was shown to protect mice against heavy infection with spores of Cl. tetani in $CaCl_2$ solution by killing the cells at the site of injection within 2 days, whereas these remained for up to 24 days in mice protected by tetanus antitoxin.

"Due to the possible occurrence of resistant strains, caution should be adopted before using antibiotics instead of antitoxin in passive prophylaxis in humans."

ORŁOWSKA, Barbara, MEDUSKI, J. & USPIENSKAJA, Wiera D. Opracowanie metody pomiarów ilościowych fosfolipazy C *Clostridium perfringens* i *Clostridium oedematiens*. [**Quantitative Determination of Phospholipase C of** *Cl. welchii* **and** *Cl. oedematiens*] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 2, 141–7, 6 figs. English summary.

BROOKS, M. Elizabeth & EPPS, H. B. G. **Taxonomic Studies of the Genus** *Clostridium*: *Clostridium bifermentans* **and** *C. sordellii*. *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 144–55, 1 pl. [38 refs.]

"In an attempt to elucidate the taxonomic relationship of *Clostridium bifermentans* and *C. sordellii* about sixty strains assigned to one or other of the two species were examined. Two groups of strains differing in their cultural and biochemical properties were recognized. One closely resembled the type culture of *C. bifermentans* (Tissier & Martelly, 1902), and the other, in which some strains were pathogenic, resembled the *C. sordellii* isolate '82' Sordelli. The former of these groups is clearly to be regarded as *C. bifermentans* and the latter as *C. sordellii*. It has been shown that the two species, although similar in many respects, are distinct and easily distinguishable. In view of this, the present practice of some bacteriologists of combining the two species under the name *C. bifermentans* is incorrect and should be discontinued."

VAN THIEL, P. H. **Are Spirochaetes Bacteria or Protozoa?** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 2, 161–8. [27 refs.]

In 1948 Van Thiel stated his reasons for regarding spirochaetes as having more affinities with protozoa than with bacteria. In the present paper he reviews more recent evidence. It is difficult to follow the arguments, which are mainly based on electron micrographs in several papers published elsewhere, and those interested will need to consult many of the references quoted. To summarize, Van Thiel's present view is that spirochaetes are derived from "a hypothetic archetype of life, next to bacteria and protozoa". From this he argues that it would be logical to classify them within the subregnum Protozoa, but he would accept their inclusion in the subregnum Bacteria. *S. T. Cowan*

MARKOVETZ, A. J. & LARSON, A. D. **Transamination in** *Leptospira biflexa*. *Proc. Soc. Exper. Biol. & Med.* 1959, Aug.–Sept., v. 101, No. 4, 638–40. [10 refs.]

SARASIN, G. Zum Organotropismus der Spirochaete *B. duttoni* gegenüber der übertragenden Zecke. [**The Organotropism of the Spirochaete** *Spirochaeta duttoni* **inside the Transmitting Tick**] *Acta Tropica*. Basle. 1959, v. 16, No. 3, 218–43, 3 figs. [21 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 38.]

BACTERIOPHAGES

PANIJEL, J. Les activités enzymatiques liées aux phages et à la synthèse phagique. [**Phage Enzymes and Enzymic Activities implied in Phage Synthesis**] *Ann. Inst. Pasteur.* 1959, Aug., v. 97, No. 2, 198–217, 1 fig. [25 refs.]

Lysates of many temperate and virulent phages contain an enzyme called prolysin which lyses acetone-dried bacteria [PANIJEL and HUPPERT, this *Bulletin*, 1958, v. 33, 76]. Some lysates also contain a substance which, in the presence of versene and sucrose, transforms bacteria into protoplasts. Again, some phage particles, in the presence of sucrose and without versene, transform the bacteria on to which they adsorb into protoplast-like structures. This paper recounts a comparative study of these properties, and of their appearance in the phage particles themselves and in the culture medium during phage synthesis.

There is evidence that the 3 properties are distinct. They differ (1) in specificity: *e.g.* lysates of phage D4 grown in *Salmonella enteritidis* changed *Escherichia coli* B, but not *Salmonella*, cells into protoplasts, although the prolysin liberated lysed both sorts of cell; (2) in time of appearance: *e.g.* prolysin was detected in T2 cultures before lysis occurred while the ability to make protoplasts appeared much later and after lysis; and (3) in their occurrence in different systems: *e.g.* lysates of phage Fcz grown on *E. coli* Fb contained prolysin but did not induce the formation of protoplasts.

T2 phage particles, on adsorption at a multiplicity of 100 and in medium containing sucrose but not versene, turned *E. coli* cells into protoplast-like structures. In the absence of sucrose, or upon dilution with water, lysis-from-without occurred. When T2 was disrupted by osmotic shock and the ghosts separated by centrifugation, prolysin remained in the supernatant fluid while

the ghosts themselves retained the ability to make protoplasts. When phage was disrupted by freezing and thawing, it lost the ability to make protoplasts, suggesting that this ability depended upon the integrity of the ghosts.

Lysates of phage Fcz grown in *E. coli* Fb displayed another property which appeared later in phage synthesis. The lysates produced a change in a cell wall antigen so that bacteria normally agglutinated by trypaflavine became inagglutinable.

The author speculates about the significance of these various activities in the phage multiplication cycle. He suggests that the difference between the factor inducing protoplast formation, which appears to be closely associated with the phage particle and is possibly an internal enzyme, and prolysin, which behaves like a superficial enzyme separable from the particle, may be reflected in their functions. The internal enzyme may play a bigger part in the penetration of the host cell wall by the phage particle at the start of infection than prolysin, which may be more concerned with the lysis of the bacterium from the inside at the time of phage maturation and release. *Janice Taverne*

HERCÍK, F. **The X-Ray Induction of Lytic Units in *Escherichia coli B*.** *Folia Biol.* Prague. 1958, v. 4, No. 2, 65–74, 1 fig. [20 refs.]

It has been reported by a Czechoslovakian worker that ultrafiltrates of cultures of *Escherichia coli* B disrupted by supersonic waves caused lysis of healthy cells of the same strain, and that this ability to cause lysis could be serially transmitted from culture to culture (HRADECNÁ, *Československá Biologie*, 1956, v. 5, 241). This paper describes the same phenomenon displayed by *E. coli* B cells subjected to X-rays.

Broth cultures of *E. coli* B, in tubes sealed to prevent phage contamination from the outside, were exposed to X-rays, the bacterial debris separated by centrifugation or filtration, and some of the supernate or filtrate added to fresh cultures of the same strain. Transmissible lysis was induced in 48% of 475 cultures tested. The extent of lysis was determined by turbidity measurements on broth cultures or by plaque development on solid medium. Complete or partial lysis occurred after a latent period of 2 hours. Lysates of normal cells made by the action of the filtrate gave 10^7 plaques per ml., rising to 10^{12} per ml. by the 4th passage. The amount of "lytic factor" produced was not consistently related to X-ray dosage. It was greatest, however, with old cultures at the beginning of the log phase of growth. Lysates examined under the electron microscope were seen to contain elongated and enlarged bacteria, empty cell membranes, and a few uniform globules possibly similar to immature phage particles.

The author discusses the nature of the "lytic factor". He thinks it unlikely to be a bacteriophage induced by X-rays because he tested *E. coli* B on 64 other strains and could find no evidence that it was lysogenic. He also excludes the possibility that lytic enzymes associated with phage development are concerned, as these are not themselves capable of serial reproduction [this *Bulletin*, 1957, v. 32, 366].

[Since this paper was published, indirect evidence for the existence of a defective prophage in *E. coli* B has been obtained by COHEN (*ibid.*, 1959, v. 34, 683).] *Janice Taverne*

CAMPBELL, A. & BALBINDER, Evelyn. **Transduction of the Galactose Region of *Escherichia coli* K 12 by the Phages λ and λ-434 Hybrid.** *Genetics.* 1959, May, v. 44, No. 3, Pt. 1, 309–19. [11 refs.]

KELLENBERGER, E., SÉCHAUD, J. & RYTER, A. **Electron Microscopical Studies of Phage Multiplication. IV. The Establishment of the DNA Pool of Vegetative Phage and the Maturation of Phage Particles.** *Virology.* New York. 1959, Aug., v. 8, No. 4, 478–98, 9 figs. [35 refs.]

The course of development of T2 phage within *Escherichia coli* B has been observed under the electron microscope in ultra-thin sections of cells fixed with osmium tetroxide at intervals during the latent period. Immediately after infection, the bacterial nucleus disintegrated. 4 minutes later vacuoles appeared at the margin of the cell; they contained fibrils, and they continued to grow until they filled the whole cell. Chloramphenicol added at the time of infection, when it is known to inhibit the synthesis of phage DNA, blocked even so early a step as the breakdown of the bacterial nucleus. At 10 minutes, before any mature phage was visible, dense phage-shaped particles were seen on the edge of the vacuoles. These dense bodies did not seem to survive lysis, as their number per cell was greater than both the number of intact phage particles and of empty heads per cell counted in lysates. Chloramphenicol added 8 minutes after infection did not affect the formation of the vacuoles nor of the dense particles.

In the presence of proflavine, the first steps in phage synthesis looked normal, but later fewer dense particles formed. Before lysis, badly filled particles, intermediate in appearance between normal whole particles and empty heads, were seen in the cells, but few of the empty heads commonly found in proflavine lysates.

The authors argue that the vacuoles consist of a pool of phage-precursor DNA. It is generally believed that the pool of precursor DNA recognized chemically can be identified with the genetic pool. The morphological pool, they suggest, can also be identified with these because (1) it looks like DNA, its structure resembling that of the bacterial nucleus, (2) it is fibrillar and (3) its increase in size runs parallel with that of chemically-determined DNA. They discuss genetic recombination between phage-precursor DNA in the light of their findings.

It is considered that the dense particles about the size and shape of phage particles seen on the edge of the vacuoles are formed by the condensation of phage DNA, which is mediated by a "condensation principle" probably protein in nature since the condensation is inhibited by chloramphenicol. The condensed DNA particles have no protein membranes, which may explain why they do not survive lysis in a recognizable form. *Janice Taverne*

LANNI, F. **Small Reversible Clumps of Bacteriophage and their Anomalous Serologic Behavior.** *J. Immunology.* 1959, Aug., v. 83, No. 2, 148–66, 4 figs. [43 refs.]

It was noticed that preparations of T5 phage which had been diluted in broth and stored at 4°C. for several weeks showed a loss of infectivity and were more sensitive to neutralization by antiserum than freshly diluted suspensions. Purified stocks stored undiluted retained their infectivity and did not change in their susceptibility to serum neutralization. On dilution, the loss of infectivity continued over several weeks till a new stable condition was reached. A non-dialysable broth component and salt were shown to be concerned. Partial infectivity was recovered however, even after storage for 2 years, if the phage was placed at 37°C. for 30 minutes and almost complete infectivity after 44°C. for 15 minutes. The phenomenon was observed with some stocks of T5 mutants and of T2, but not with stocks of T1, T3 and T4.

The changes in property of phage stocks diluted and stored at low temperatures were shown statistically to be caused by the formation at 4°C. of clumps of phage which dissociated at higher temperatures. The broth factor may act either as a nucleus around which a clump forms, or as a bonding agent. Plaques caused by clumps were smaller than those arising from free phage, and it is thought the clumps were not infective until they dissociated. Clumps subjected to the action of a Waring blendor fragmented without recovery of infectivity. The clumps appeared to consist of fewer than 10 particles on average, and to be fairly uniform. The author suggests that the tails of the clumped phage particles are directed inwards. This would explain the loss of infectivity. The size of clumps would be uniform because of steric hindrance limitations. Clumps of phage might be more sensitive to serum neutralization than free phage because any antibody molecules, including those specific for the phage head which do not neutralize, might react with adjacent particles in a clump and prevent their dissociation. *Janice Taverne*

READ, K. S. & FERGUSON, W. W. **Plaque Type Variation in Temperate Phages of** *Salmonella typhosa.* *J. Bacteriology.* 1959, Aug., v. 78, No. 2, 295–6, 1 fig.

This note reports the isolation of virulent mutants from 9 different Vi phages of *Salmonella typhi.* When plated on a non-lysogenic host such as Vi-phage type A of *Salm. typhi,* the mutants gave rise to clear plaques, distinguishable from the turbid plaques produced by the temperate stock. "An exact ratio between turbid and clear plaque mutants has not been determined but the initial difference is thought to be more than 1000:1." *Janice Taverne*

TAKEYA, K., MORI, R., UEDA, S. & TODA, T. **Bacteriophage of** *Pseudomonas aeruginosa* **with Unfamiliar Head Morphology.** *J. Bacteriology.* 1959, Sept., v. 78, No. 3, 332–5, 6 figs.

ORTEL, S. Elektronenoptische Untersuchungen an Staphylokokken-Bakteriophagen. [**Electron Microscopical Examination of Staphylococcus Phages**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 176, Nos. 1/2, 35–49, 11 figs. on 6 pls.

The English summary appended to the paper is as follows:—

"The electron microscopical examination of staphylococcus phages revealed a variety of morphological structures. The phage head may be round or elongated, the tail of different length. Phage strains used for the typing of a special group may show different morphological characters."

KELLER, R. & ZATZMAN, M. L. **Studies on the Factors concerned in the Disappearance of Bacteriophage Particles from the Animal Body.** *J. Immunology.* 1959, Aug., v. 83, No. 2, 167–72, 1 fig. [21 refs.]

A phage derived from *Bacillus megaterium* having a head width of 49 mμ was injected intravenously into 18 dogs and arterial blood assayed for phage at intervals after injection. The rate of disappearance of the phage was greater than could be accounted for by dilution alone. It was rapid during the first 15 minutes but later declined more slowly, suggesting that several factors were concerned. One factor, it is proposed, may be the properdin system, as normal serum neutralized up to 55% of the phage in 10 minutes *in vitro.* Much of the phage appears to be removed by the reticulo-endothelial system. Spleen and liver samples were homogenized, their phage content assayed and the phage concentration factors calculated. Both organs were found to be filtering phage from the circulation, as they do bacteria. However, no appreciable change in the phage disappearance curve occurred in dogs which had undergone splenectomy. The kidney did not concentrate phage, although the particles were able to cross the renal barrier. Phage assays on urine samples indicated that phage was excreted at a rate which depended on concentration and which was consistent with a process governed by diffusion. *Janice Taverne*

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Enteric group; Arthropod-borne group; Others.**

SOCIETY FOR GENERAL MICROBIOLOGY. **Virus Growth and Variation. Ninth Symposium of the Society for General Microbiology held at the Senate House, University of London, April 1959.** pp. viii + 272, numerous illustrations. 1959. London: Cambridge University Press, Bentley House, 200, Euston Road, N.W.1. [35s.]

This volume contains the papers presented at the 9th symposium of the Society for General Microbiology, held in London in April 1959 and devoted to the consideration of the growth and variation of viruses, and in particular to knowledge which has accumulated since the symposium on a similar topic held in 1952 [this *Bulletin*, 1953, v. 28, 989]. In an introductory address, S. E. LURIA (pp. 1–10) points out that advances in knowledge have been mainly in the field of cellular biology and that advances in practical virology still lie in the future. The replication of phage is discussed by E. KELLENBERGER (pp. 11–33), who postulates that a condensation principle is necessary for bringing about the condensation of the pool of newly formed deoxyribonucleic acid into mature phage particles. In a paper on the multiplication of viruses which contain ribonucleic acid W. SCHÄFER (pp. 61–81) describes incomplete forms associated with fowl plague virus which resembled microsomes in their morphology, could be adsorbed to and eluted from chick red cells, and possessed glucose-6-phosphatase activity. The phenotypic mixing of strains of virus possessing different markers is discussed by G. K. HIRST (pp. 82–101); with Newcastle disease virus, attempts to produce recombination have been unsuccessful, but evidence has been obtained of the existence of a diploid state in this virus. A review of work on interferon is given by A. ISAACS (pp. 102–121). Investigations of its chemical nature have shown that it is inactivated by pepsin but not by nucleases or receptor-destroying enzyme, and is presumably a protein not associated with nucleic acid or carbohydrate. The growth cycle of herpes virus in HeLa cells is described by M. G. P. STOKER (pp. 142–170), and other topics of medical interest dealt with in subsequent papers include studies of the growth of vaccinia virus by H. B. MAITLAND and R. POSTLETHWAITE (pp. 185–199), and an informative and well-illustrated account of the adenoviruses by C. MORGAN and H. M. ROSE (pp. 256–272).

D. J. Bauer

STULBERG, C. S., RIGHTSEL, W. A., PAGE, R. H. & BERMAN, L. **Virologic Use of Monkey Kidney Cells preserved by Freezing.** *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 415–18, 2 figs.

It has been found possible to preserve freshly trypsinized monkey kidney cells and also cells removed by versene from a monolayer obtained by the growth of such freshly trypsinized cells, by freezing them slowly to −75°C. in 80% Eagle's basal medium, 15% calf serum and 5% glycerol. The cells were thawed rapidly under running water at 37°C. and were then diluted to an appropriate cell concentration in growth medium consisting of Eagle's basal medium and 5% calf serum. The cells were frozen in such a concentration that at least a 1/10 dilution could be made after thawing so that the glycerol could be removed by dilution rather than washing.

The recovery of viable cells was about 70%; the cells which had been grown as a monolayer preserved better than freshly trypsinized cells. If the medium contained 2·2 gm./litre of sodium bicarbonate it was found advantageous to use 5% CO_2 in the atmosphere but this was not necessary if the bicarbonate content was lowered to 0·35 gm./litre. The frozen and thawed cells took about a day longer to reach a confluent monolayer than freshly prepared unfrozen cells. The monolayer cultures produced from the frozen and thawed cells were as sensitive to enteroviruses, adenovirus, influenza virus, herpes simplex, measles and some of the newer respiratory viruses, for example CA, HA-1, JH and 2060, as were those from unfrozen cells. The cultures were not only sensitive for primary isolation but were also as sensitive in parallel titrations of the viruses when assayed by tube titration or plaque formation, indeed for some viruses the titres were significantly higher in frozen and thawed cells. The authors point out the advantages of being able to preserve cells while a portion of the batch is tested for the presence of simian virus infection.

A. J. Beale

VALENTINE, R. C. & ALLISON, A. C. **Virus Particle Adsorption. I. Theory of Adsorption and Experiments on the Attachment of Particles to Non-Biological Surfaces.** *Biochim. et Biophys. Acta.* 1959, July, v. 34, No. 1, 10–23, 3 figs. [25 refs.]

"It has been shown experimentally that even in a shaken system the rate at which virus and similarly sized particles in suspension arrive at a surface can be accurately predicted from the theory of Brownian motion. Equations are deduced from which the rate of arrival of particles on flat and spherical surfaces can be calculated. Experiments with various non-biological surfaces have shown that all the impinging particles are adsorbed when a sufficient concentration of ions is present. The effects of various concentrations of different salts on rates of particle adsorption have been investigated. It is concluded that the results are at variance with current theories of particle-surface interactions. They also suggest that a considerable delay in the start of a virus infection may result from the long time needed for the virus to reach a cell surface."

QUERSIN-THIRY, Lise. **Action of Anticellular Sera on Virus Infections. II. Influence on Heterologous Tissue Cultures.** *J. Immunology.* 1959, June, v. 82, No. 6, 542–52, 6 figs. [20 refs.]

This is an important paper which should be read in the original by all who are interested in the origin of the

recently described continuous cell lines. The author [this *Bulletin*, 1959, v. 34, 91] has previously shown that heat inactivated rabbit antisera against various cells cause agglutination of those cells at low dilutions and lysis in the presence of complement. At higher dilutions the anticellular sera protect the cells against the action of viruses; this protection is high for some viruses, for example ECHO 9, and moderate against others, for example polioviruses, and very weak against yet other viruses, for example Coxsackie B or Newcastle disease virus. These 2 measures (agglutination and protection against viruses) of the action of anticellular sera have been used for an antigenic analysis of 23 continuous cell lines of widely divergent origin and also of various primary cell cultures.

The results can be explained on the assumption that there are 2 cellular antigens, one common to all cells of human or simian origin and another common to all cells sensitive to poliovirus. Thus complete cross reactions always occur between the human cell lines, HeLa, KB, T, N, LoFi, C, HL and Salk's monkey heart line. The only human cell lines that do not completely cross react are U12 (a strain of normal human uterus first isolated by SWIM and PARKER (*Proc. Soc. Exper. Biol. & Med.*, 1955, v. 89, 549)), Lung TO (a strain of human embryo lung isolated by HENLE and DEINHARDT (*J. Immunol.*, 1957, v. 79, 54)), and the FS (a strain of human foreskin also first isolated by Swim and Parker). All these strains are of human origin but are not susceptible to poliovirus. There are also strains of monkey kidney cells isolated by Dr. Parker in Canada which share the primate antigen but lack the antigen associated with poliovirus susceptibility. On the other hand, non-primate cells which are susceptible to poliovirus, for example ERK cells first isolated by WESTWOOD *et al.* [this *Bulletin*, 1957, v. 32, 815] and a rabbit spleen cell line, also isolated by Dr. Westwood, share the antigen associated with poliovirus susceptibility but lack that associated with primate tissue and therefore give partial cross reactions with primate cell antisera. The only exception to these findings is that 3 different sub-lines of the L strain of mouse fibroblasts have some slight cross reactions with anti-HeLa and anti-U12 antiserum, that is to say they cross with the primate component of human cells. During the first week of growth of trypsinized monkey kidney cells they acquire an antigen that is associated with poliovirus susceptibility. They also acquire this antigen when grown as homografts.

Antiserum prepared from monkey kidney organs reacts only weakly with stable continuous cell lines that are of human origin. Occasional differences were noted between strains in their relative ability to be agglutinated or protected by anticellular sera and also in their capacity to evoke good antisera in animals. Thus, for example, Chang's human liver line (HL) is particularly susceptible to agglutination but less easily protected against virus action, but anti-HL serum, on the other hand, has very weak powers of agglutination but a particularly high protective effect on all the cells which are of primate origin and susceptible to poliovirus. These findings provide a tool which enable the cell lines to be distinguished from one another and would appear to show clearly that the cells of non-primate origin which are susceptible to poliovirus are distinct from the cells of primate origin that are susceptible to poliovirus. They do not support the view that such non-primate poliovirus susceptible cells are the result of laboratory contamination. *A. J. Beale*

PORTERFIELD, J. S. **A Simple Plaque Inhibition Test for Antiviral Agents: Application to Assay of Interferon.** *Lancet.* 1959, Sept. 12, 326–7, 3 figs. [10 refs.]

A monolayer of chick embryo cells is infected with virus, then overlaid with agar containing nutrients and neutral red. Interferon is then placed on the surface in "fish-spines". The interferon diffuses into the agar and protects a surrounding zone of cells from destruction by the virus. The diameter of the zone was found to be inversely proportional to the dose of virus and the area of the zone was directly proportional to the logarithm of the concentration of interferon.

With yellow fever and influenza viruses the boundary of the zone was not sharp, but boundaries were very well defined with Bunyamwera virus. Larger zones were formed with West Nile and Bunyamwera viruses than with the more rapidly multiplying western equine encephalomyelitis virus. Interferon prepared in chick embryo cells inhibited vaccina virus, but inhibition could not be demonstrated with interferon prepared in rabbit kidney cells. Greater precision in assay of interferon can be obtained by the use of large trays on which 36 or 64 samples can be examined under identical conditions. Bunyamwera virus appears to be a particularly suitable test organism. *C. E. Gordon Smith*

CAMPILLO SAINZ, C. & NEGRETE, Ana M. Vacuna antivariólica preparada en cultivo de tejidos de riñón de conejo. **[Smallpox Vaccine prepared in Rabbit Kidney Tissue Culture]** *Bol. Oficina Sanitaria Panamericana.* 1959, Sept., v. 47, No. 3, 228–31.

The English summary appended to the paper is as follows:—

"The article describes the preparation of a smallpox vaccine obtained with tissue of rabbit kidney. This bacteriologically sterile product, because it is so inexpensive and easy to prepare, appears to be superior to any other similar products in use for the prevention of human smallpox. The number of doses obtained when using the kidneys of a rabbit equals those obtained from a calf. A preliminary field test was made in 102 unvaccinated individuals. Of these, 95 (93 per cent) showed primary takes which, in time of appearance, evolution, and characteristics, were similar to those produced with calf's lymph."

FENNER, F. **Genetic Studies with Mammalian Poxviruses. II. Recombination between Two Strains of Vaccinia Virus in Single HeLa Cells.** *Virology.* New York. 1959, Aug., v. 8, No. 4, 499–507.

After exposing HeLa cell monolayers to very heavy mixed infections with 2 different strains of vaccinia virus, the cultures were broken up by trypsinization and 33 single cells incubated for 36 hours in microdrops of

tissue culture medium. At the end of this period each cell was frozen and thawed in 1 ml. of gelatin saline and then treated with an ultrasonic drill for 30 seconds before being titrated on chick embryos. Yields of infectious virus per HeLa cell varied between 0 and 493; the average yield was 87. 325 clones of virus from 10 cells were examined; 218 were parental type and 106 showed various mixtures of parental characters. [1 clone from cell number 19 seems to have got lost.] Most of the cells which produced recombined virus produced more than 1 phenotype.

[For Part I, see this *Bulletin,* 1958, v. 33, 1091.]

Colin Kaplan

YOUNGNER, J. S. & RUBINSTEIN, Gayle. **Separation of a Soluble Hemagglutinin from Vaccinia Virus by a Flotation Method.** [Correspondence.] *Virology.* New York. 1959, July, v. 8, No. 3, 386–8.

Extracts of chorioallantoic membranes infected with vaccinia virus were clarified by centrifugation. The density of the fluid was adjusted to about 1·06 by the addition of NaCl, and it was then centrifuged at high relative centrifugal force. 3 fractions were distinguishable from above downwards: a cream, a clear fluid and a pellet of deposit. All three were tested for haemagglutinating ability. Haemagglutinin (HA) was present in both cream and deposit, but not in the clear fluid. In several experiments about 80% of the HA was recovered in the sediment, the remaining 20% in the cream was regarded as soluble haemagglutinin (SHA). SHA was heat labile, while HA associated with the deposit (elementary bodies) was heat stable at 56°C. for 30 minutes. SHA activity was increased 64-fold after incubation with 0·5 trypsin for 30 minutes at 37°C. SHA contains 40% protein and 40% lipid.

Colin Kaplan

BRIODY, B. A. **Response of Mice to Ectromelia and Vaccinia Viruses.** *Bact. Reviews.* 1959, June, v. 23, No. 2, 61–95, 1 fig. [38 refs.]

This rather long paper considers the epidemiology of ectromelia in mouse colonies in the United States. The author goes fully into the aetiology and pathogenesis of the disease, and discusses methods of diagnosis and control. He points out the advantages of using the vaccinia haemagglutination inhibition test to determine the presence of enzootic or epizootic infection with ectromelia virus in mouse stocks. Both may be controlled rapidly by destroying all overtly diseased animals and vaccinating the rest by scarification of the base of the tail through a small drop of vaccinia virus suspension. The strain of vaccinia virus particularly recommended for immunizing mice is known as IHD-T. It does not induce the formation of haemagglutinin inhibiting antibody. The haemagglutination inhibition test may, therefore, be used in monitoring vaccinated colonies for the presence of ectromelia virus.

[It is difficult to summarize the mass of information in this paper. It should undoubtedly be read by everyone who uses mice for experimental work.] *Colin Kaplan*

HANAFUSA, T., HANFUSA, H. & KAMAHORA, J. **Transformation of Ectromelia into Vaccinia Virus in Tissue Culture.** [Correspondence.] *Virology.* New York. 1959, Aug., v. 8, No. 4, 525–7, 2 figs.

Ectromelia virus produces no lesion when injected intradermally in rabbits while vaccinia virus produces a flat, hard lesion. Intraperitoneally in mice, ectromelia kills within 8 days while vaccinia virus is without apparent effect.

Monolayers of Earle's L cells were exposed to 1 ml. of infectious ectromelia virus and 1 ml. of heat-inactivated vaccinia virus. The culture fluid 48 hours later showed the characteristics of vaccinia virus. 5 experiments gave similar results. The mixture of viruses in tissue culture fluid was purified by 2 single plaque isolations: it was not pathogenic when inected intraperitoneally in mice. *Colin Kaplan*

VON MAGNUS, P., ANDERSEN, Else K., PETERSEN, K. B. & BIRCH-ANDERSEN, A. **A Pox-Like Disease in Cynomolgus Monkeys.** *Acta Path. et Microb. Scandinavica.* 1959, v. 46, No. 2, 156–76, 12 figs. [27 refs.]

DEIBEL, R. & HOTCHIN, J. E. **Quantitative Applications of Fluorescent Antibody Technique to Influenza-Virus-Infected Cell Cultures.** *Virology.* New York. 1959, July, v. 8, No. 3, 367–80, 5 figs. [15 refs.]

The fluorescent antibody technique was used for the study of quantitative aspects of interactions between the influenza virus (PR8 and Asian strains) and cultured cells of chick embryo, human amnion and calf kidney tissues. Variations on adsorption time, inoculum size, virus strain and cell type were correlated with the proportion of cells specifically stained after an adequate period of incubation. The rate of virus adsorption was highest during the first 10 minutes of contact with the cells and then progressed at a lower rate, being still incomplete after a period of 2 hours. Addition of antiserum to the virus material before inoculation prevented the development of fluorescent-stainable cells. Addition of antiserum at varying periods after infection indicated that a considerable proportion of adsorbed virus could be neutralized during the first half-hour of the infectious process but not 4 hours later. The different cell types investigated varied in capacity to support virus multiplication and in susceptibility to infection as revealed by the development of fluorescent-staining antigen. Infection of chick embryo and human amnion cells by Asian influenza virus could be shown by the fluorescent antibody technique but was not accompanied by demonstrable liberation of infective virus. Infection of calf kidney cells by the same virus strain resulted, however, in a relatively low proportion of fluorescent-stained cells and a measurable increase of infective virus. The relationship between multiplicity of exposure (expressed as log EID50 per cell) and percentage of fluorescent cells followed approximately a Poisson distribution. Advantages and limitations of the fluorescent antibody technique applied to the study of virus cell interactions are discussed *H. G. Pereira*

LIND, Patricia E. **Further Studies of an Avirulent Mutant of the Influenza A Strain WS −.** *Australian J. Exper. Biol. & Med. Sci.* 1959, Apr., v. 37, Pt. 2, 163–75. [14 refs.]

A non-virulent mutant (aWS −) of the influenza virus strain WS − has been previously described [LIND and BURNET, this *Bulletin*, 1958, v. 33, 1187]. A study of the behaviour of aWS − inoculated into mice by the intranasal route showed that this strain is adsorbed to mouse lung at the same rate as WS − but fails to proliferate on this site or to cause "toxic" congestive lung tissues when inoculated in large doses. Mice inoculated with aWS − strain were protected against subsequent challenge by WS−. Protected mice developed haemagglutination-inhibiting and neutralizing WS − antibodies but no development of influenza A complement-fixing antibodies could be demonstrated. The latter antibody appeared, however, after challenge with WS −.

Recombination experiments between aWS − and WS− were conducted in de-embryonated eggs and gave rise to strains of intermediate mouse virulence.

H. G. Pereira

PORTOCALA, R., BOERU, V. & SAMUEL, I. **Biosynthesis of Influenza Virus starting from an Ether-Phenol Virus Extract.** *Acta Virologica.* Prague. 1959, July, v. 3, No. 3, 172–4.

Partially purified preparations of an influenza virus (strain T) containing A and A-prime antigens were treated by ether followed by saturated phenol. The resulting ribonucleic acid (RNA) was shown to be infective when tested in fertile eggs but not in mice. The virus present in allantoic fluids of eggs inoculated with infective RNA, differed from the original in antigenic constitution (absence of A-prime antigen) and in morphology, showing filamentous forms which were not seen in the original strain. *H. G. Pereira*

HENDERSON, J. R. & KEMPF, J. E. **Intracellular Proteins associated with the Synthesis of the Influenza A Virus.** *Virology.* New York. 1959, Sept., v. 9, No. 1, 72–83, 2 figs. [22 refs.]

DEICHMAN, G. I. & SMORODINTSEV, A. A. **Studies of the Mechanism of Multiplication of Influenza Virus.** *Acta Virologica.* Prague. 1959, July, v. 3, No. 3, 129–38, 11 figs. [14 refs.]

The multiplication rate of influenza viruses in fertile eggs was studied by measuring infectivity and haemagglutination titres either in pooled materials from several eggs or in samples collected from individual eggs at varying periods of incubation. Growth curves obtained by the first method revealed "steps" of varying magnitude occurring at rather irregular intervals. By the second method, virus multiplication was shown to follow an exponential curve. (No precautions were taken to limit virus multiplication to single cycles.) Virus concentration in individual eggs tested at different times varied considerably. Length of latent period was inversely related to size of virus inoculum and to temperature of incubation in the range of 31 to 37°C.

H. G. Pereira

SOKOL, F. & SZURMAN, J. **Isolation of Ribonucleic Acid from Purified Influenza Virus Preparation by Phenol Extraction.** *Acta Virologica.* Prague. 1959, July, v. 3, No. 3, 175–80, 3 figs. [10 refs.]

A preparation of Asian influenza virus, purified by red cell adsorption and elution and differential centrifugation was extracted first by ether and then by saturated phenol. The aqueous phase obtained gave a UV absorption spectrum characteristic of nucleic acid. After further purification by alcohol precipitation, this material was treated by ribonuclease which caused a progressive increase of optical density at 258 mμ. The same material gave a positive orcinol test for pentoses.

Attempts to demonstrate infectivity of the virus ribonucleic acid for eggs and tissue cultures gave negative results. *H. G. Pereira*

TAKÁTSY, G., BARB, K. & FARKAS, E. **A New Erythrocyte Receptor with Exclusive Affinity to Avid Asian Strains of Influenza A Virus.** *Acta Virologica.* Prague. 1959, v. 3, Suppl., 79–84.

Red cell receptors for avid strains of Asian influenza virus were found to differ in several respects from those reacting with non-avid Asian strains or with A, A-prime and B influenza strains. The receptors for avid Asian strains resisted the action of purified receptor-destroying-enzyme (RDE), of KIO_4 and of other influenza virus strains. The avid strains are readily adsorbed onto and partially eluted from red cells pre-treated with RDE or KIO_4. Elution takes place at 37°C. but not at 4°C.

Chick embryo chorio-allantoic membranes doubly infected with avid and non-avid Asian strains yielded both virus variants in approximately equal titres. Pre-treatment of chorio-allantoic membranes with KIO_4 reduced the yield of both variants to the same extent.

H. G. Pereira

POLYAK, R. I., LUZYANINA, T. I. & SMORODINTSEV, A. A. **Biochemical Investigations of Influenza Virus Neutralizing Protein Fractions of Sera from Different Animals.** *Acta Virologica.* Prague. 1959, v. 3, Suppl., 61–70. [13 refs.]

Normal rabbit, guineapig, mouse and rat sera were found to contain a thermolabile factor capable of neutralizing mouse-virulent strains of influenza A virus. This activity was associated with serum fraction III_0 obtained by Cohn's technique (COHN *et al., J. Amer. Chem. Soc.*, 1950, v. 72, 465) from normal rabbit, guineapig and mouse sera but could not be isolated from rat sera treated by the same method. Virus-neutralizing and haemagglutinating-inhibiting activities were both present in rabbit, guineapig and mouse whole serum and fraction III_0 whereas no haemagglutinin inhibitor

could be demonstrated in rat sera. Neutralizing titres were highest in rabbit and guineapig sera and very low and variable in rat sera.

The neutralizing factor present in III_0 serum fractions had electrophoretic mobility similar to that of gamma globulin and was readily destroyed by trypsin. Its heat resistance was increased with decreasing ionic strength of the suspending medium.

Evidence is presented which suggests that this virus neutralizing factor is not identical with properdin.

H. G. Pereira

STYK, B., KOCISKOVÁ, D. & BLASKOVIC, D. **Dynamics of Immunological Response to Infection with Asian Type (A2) Influenza Virus Strains.** *Acta Virologica.* Prague. 1959, v. 3, Suppl., 97–106, 9 figs.

Antibody responses were studied in mice inoculated with single and multiple doses of avid and non-avid strains of Asian (A2) influenza virus. Antibodies formed in response to single virus inoculation were shown to be thermolabile when non-avid strains were used as antigens in haemagglutination-inhibition or virus-neutralization tests. The thermolabile character of the antibodies was less evident in sera from animals inoculated with multiple virus doses. The activity of heated sera could be restored by the addition of unheated normal sera. When avid strains were used as antigens in serological reactions the thermolabile character of antibodies could not be demonstrated. Control experiments excluded the possible role of non-specific virus inhibitors in the tests described.

It is suggested that the reaction of non-avid strains with antibody is mediated by a thermolabile co-factor present in normal sera. *H. G. Pereira*

TAKÁTSY, G. & BARB, K. **On the Normal Serum Inhibitors for the Avid Asian Strains of Influenza Virus.** *Acta Virologica.* Prague. 1959, v. 3, Suppl., 71–7. [12 refs.]

The properties of a normal serum factor capable of inhibiting the haemagglutinating activity of avid strains of Asian influenza virus are described. It occurs in high titres in normal human, rabbit, guineapig, chicken and ferret sera and in lower titres in mouse sera. Its action is enhanced by boiling for 30 minutes and, in the case of guineapig serum, by heating at 56°C. for 30 minutes. The boiled inhibitor is non-dialysable, biuret positive, precipitated by 50% acetone or 66% ethanol and inactivated by trypsin. Purified preparations obtained by precipitation with ammonium sulphate are free of detectable carbohydrate. In sera heated at 56°C. for 30 minutes its action is not affected by periodate but, with the exception of guineapig serum inhibitor, is reduced by treatment with crude filtrates of *V. cholerae*.

Normal human and guineapig sera were also shown to neutralize the infectivity of avid but not of non-avid strains of Asian influenza virus. The neutralizing titres of normal human sera were reduced by boiling but those of normal guineapig sera were not affected by this treatment. *H. G. Pereira*

HARBOE, A., REENAAS, R. & OPPEDAL, M. **Studies on Francis Inhibitor of Influenza Virus Haemagglutination in Rabbit Serum Fractions obtained by Electrophoresis on Starch-Grain.** *Acta Path. et Microb. Scandinavica.* 1958, v. 44, No. 1, 92–105, 1 fig. [32 refs.]

HÁNA, L. & STYK, B. **Some Properties of Influenza C Virus Haemagglutination Inhibitor from Rat Serum.** *Acta Virologica.* Prague. 1959, v. 3, Suppl., 85–90, 3 figs. (2 on 2 pls.). [23 refs.]

The haemagglutinating activity of influenza C virus is inhibited by a thermostable factor (C-inhibitor) present in normal rat serum. This inhibitor is not destroyed by *Vibrio cholerae* receptor-destroying enzyme. Its electrophoretic mobility at *p*H 9·0 corresponds to that of serum alpha globulin. At *p*H 4·6 the inhibitor moves faster towards the anode than albumins and globulins. The content of hexosamines, hexoses and neuraminic acid of serum fractions obtained by paper electrophoresis was correlated with haemagglutinating-inhibiting activity. These findings suggest that C-inhibitor is a glycoprotein.

H. G. Pereira

LAUCÍKOVÁ, O., with the technical assistance of A. FASUNGOVÁ. **Enzymatic Split Product of Influenza Virus Haemagglutination Inhibitor.** *Acta Virologica.* Prague. 1959, Ju'y, v. 3, No. 3, 139–44, 2 text figs. & 3 figs. on pl. [16 refs.]

The action of receptor-destroying enzyme (RDE) and of influenza virus on the haemagglutination-inhibitor isolated from chick embryo chorio-allantoic membranes was studied by biological and chemical methods. The amount of sialic acid split from the inhibitor by the action of RDE or influenza virus was estimated by Dische's diphenylamine reaction and found to be proportional to the drop of haemagglutination-inhibiting activity. The split product was identified by paper chromatography as N-acetylneuraminic acid.

H. G. Pereira

WEN, Hsi-Shan & WANG, San-Pin. **Mouse Adaptation of the Asian Influenza Virus.** *J. Infect. Dis.* 1959, July–Aug., v. 105, No. 1, 9–17, 3 figs. [12 refs.]

Adaptation of Asian influenza virus to multiply in the lungs of several inbred mouse strains was achieved by serial passages by the intranasal route. Lesions observed on first passage consisted of pulmonary consolidation of a "toxic" character. Subsequent passages gave rise to minimal lesions associated with low levels of virus multiplication until the 7th to 10th passages, after which lesions and virus titres were considerably increased, resulting in occasional deaths. The lesions observed after adaptation were similar to those caused by other mouse-adapted influenza viruses.

H. G. Pereira

ABINANTI, F. R. & HUEBNER, R. J. **The Serological Relationships of Strains of Parainfluenza 3 Virus isolated from Humans and Cattle with Respiratory Disease.** [Correspondence.] *Virology.* New York. 1959, July, v. 8, No. 3, 391–4.

A haemadsorption virus was isolated from nasal secretions of cattle suffering from a respiratory syndrome called "shipping fever". The biological properties of this virus are comparable to those of parainfluenza 3 virus (type 1 haemadsorption virus). The 2 viruses were also shown to resemble each other closely in antigenic constitution. *H. G. Pereira*

NOICE, F., BOLIN, F. M. & EVELETH, D. F. **Incidence of Viral Parotitis in the Domestic Dog.** *J. Dis. Children.* Chicago. 1959, Sept., v. 98, No. 3, 350–52.

"Two dogs examined were found to have severe parotitis, one of the dogs, No. 8-450A, being positive for mumps virus by the complement-fixation test. In both cases processed saliva specimens revealed a virus capable of killing embryonated hens' eggs and was inhibited for its hemagglutination properties by a standard human mumps antiserum. From one case a cytolytic virus was isolated, with use of HeLa cell tissue cultures. The virulence in vitro appeared to decrease with progressive subpassages to a point of no cytolytic activity."

PEREIRA, Marguerite S. & PEREIRA, H. G. **Coe Virus. Properties and Prevalence in Great Britain.** *Lancet.* 1959, Oct. 10, 539–41, 2 figs. [10 refs.]

LENNETTE *et al.* [this *Bulletin*, 1959, v. 34, 397] described the isolation, in HeLa cell culture, of a virus which they named Coe, from sporadic cases of respiratory disease. Strains of this virus have now been isolated from 4 persons during a trial of adenovirus vaccine in the Royal Air Force. The patients suffered from fever, pharyngitis and cough. The virus was isolated from throat swabs in HeLa cells, degeneration being observed between 10 and 16 days after inoculation. The virus would also grow in human amnion cells and embryonic rabbit kidney cells. The cytopathic effect and the appearance of plaques on HeLa cells are illustrated. The virus did not grow in monkey kidney cells or in chick embryos. Occasional suckling mice were paralysed, but serial passage was unsuccessful. The virus resembled enteroviruses in size (approximately 20 mil imicrons in diameter) and resistance to ether. Similar enteroviruses have been isolated in HeLa cells from the alimentary canal of patients with respiratory diseases by KASEL *et al.* [this *Bulletin*, 1959, v. 34, 587]. The 4 strains isolated in England were identical serologically with Coe virus and were unrelated to poliovirus 1–3, Coxsackie B 1–5 and A9 and ECHO virus types 1–14.

A small serological survey was carried out [the method of selecting the sera is not given] from which it was concluded that Coe virus infection increases with age and is more prevalent in men than in women. Evidence supporting the view that military training offers opportunities for Coe virus infection is promised. *A. J. Beale*

CHADWICK, D. L., WELSH, H. H. & LENNETTE, E. H. **Comparison of the Sensitivity of Several Mammalian Cell Types for the Isolation of Poliomyelitis Viruses from Man.** *J. Lab. & Clin. Med.* 1959, Sept., v. 54, No. 3, 409–16. [11 refs.]

"An inquiry was made into the comparative sensitivity of monkey kidney, strain HeLa, strain KB, and human amnion cells in the detection of poliomyelitis viruses in stool suspensions. Essentially no difference was found in the efficiency of these 4 cell systems in the recovery of these viruses. The clinical specimens tested contained only type 1 or type 3 viruses.

"Monkey kidney cells appeared to be somewhat more resistant to the effects of toxic factors in stool suspensions than were the other cell systems employed, but the difference was not found to be statistically significant.

"The choice of the cell system to be employed for isolation of poliomyelitis viruses will depend on practical local considerations."

ALBANO, A. **Cultivation of HeLa Cells in Calf Serum and the Susceptibility of Such Cells to Polio- and Adenoviruses.** *Acta Path. et Microb. Scandinavica.* 1958, v. 44, No. 3, 307–12, 2 figs. [16 refs.]

"The propagation of HeLa cells in calf serum medium is described. The cells are as susceptible to the cytopathogenic effects of polio- and adeno-viruses and as efficient in supporting multiplication of these viruses as are cells grown in human serum."

DARNELL, J. E., Jr., EAGLE, H. & SAWYER, T. K. **The Effect of Cell Population Density on the Amino Acid Requirements for Poliovirus Synthesis in HeLa Cells.** *J. Exper. Med.* 1959, Sept. 1, v. 110, No. 3, 445–50, 1 fig. 15 refs.]

The authors have previously shown, using HeLa cells grown as monolayers, that the only components of the cell growth medium that are required for the maximum output of poliovirus are glucose, glutamine and salts [Darnell and Eagle, this *Bulletin*, 1959, v. 34, 293]. The present experiments were designed to answer the question as to whether the newly formed poliovirus is derived from the free amino acid pool of the cells or whether from cell protein which is broken down. The experiments were done with HeLa cells grown in suspension with a multiplicity of infection of about 20–30 plaque-forming units of the Mahoney strain of type 1 poliovirus. It was found that the growth cycle of poliovirus in suspended cells was the same as for monolayer cultures. Virus maturation began within 4 hours and was virtually complete within 8 hours

although virus was not released into the surrounding medium until 18 to 24 hours after infection. With high cell densities (5×10^5 cells/ml.) the yield of poliovirus in salt solution supplemented with glucose and glutamine closely approached that obtained in a complete growth medium. When the cell density was reduced 10-fold the addition of glucose and glutamine was quite inadequate to restore poliovirus production, thus only 9 plaque forming units per cell were produced on medium containing glucose and glutamine as against 265 in the complete growth medium. When the cell density was reduced to 5×10^3 cells/ml. the yield of poliovirus became very erratic but in complete growth medium an average of 238 plaque forming units per cell were produced. The highest yields per cell, in the region of 400–500 plaque forming units per cell, were obtained with the highest cell density and either complete growth medium or glucose and glutamine plus the essential amino acids or with the lowest cell density when glucose, glutamine, the essential amino acids and either 3% dialysed horse serum or 1% buffered serum albumin were used. The experiments support the conclusion that the poliovirus is produced from the amino acid pool. The exact role of bovine serum albumin or dialysed horse serum in boosting the yield of poliovirus per cell in depleted cells is uncertain. *A. J. Beale*

Jezierski, A.; Adriaensens, J. Atténuation des trois types de virus de la poliomyélite sur les tissus de singes de l'espèce Colobus. Virus vivants modifiés et leur application par différentes voies sur les singes. I. Administration par voie orale aux chimpanzés et à l'homme [Jezierski]. *Ann. Soc. Belge de Méd. Trop.* 1959, Feb. 28, v. 39, No. 1, 69–84. II. Administration par voie orale des virus vivants modifiés de la poliomyélite à des volontaires humains. Essais préliminaires [Jezierski & Adriaensens]. [**Attenuation of the 3 Types of Polio Virus in Colobus Monkey Tissue Culture. Application to Monkeys by Different Routes. I. Oral Administration of Attenuated Strains to Chimpanzees. II. Oral Administration to Volunteers**] *Ibid.*, 84–94. [32 refs.]

I. Attenuated strains of all 3 types of poliovirus were obtained by serial passage in fibroblast cultures from testicular tissue of Colobus monkeys. There was a gradual diminution of virulence on passage. The 148 passage virus of all 3 types was found to be non-pathogenic for several species of Central African monkeys by the intracerebral, intraspinal and intramuscular routes. The individual types (10^7 TCD50 for type 1 and 10^6 for types 2 and 3 in 1 ml.) of virus and the three mixed together were fed to groups of chimpanzees. The animals remained healthy and did not have a viraemia. Virus excretion was constant as was antibody response when individual types were given separately. The response to the mixture appeared satisfactory when given in a 3 ml. dose.

II. As a result of these satisfactory results 21 human volunteers between the ages of 12 and 21 were fed these attenuated strains. 7 received type 1, 6 type 2, 6 type 3, and 2 a mixture of all 3 types. Virus excretion was noted in all individuals, regardless of the pre-feeding antibody titre (these were in the range of undetectable to 1/32). The antibody responses were in general encouraging, all the individuals fed only 1 virus showing an antibody response (titre range 1/5–1/320). The response to the trivalent mixture was definite but less good. *A. J. Beale*

Likar, M., Bartley, E. O. & Wilson, D. C. **Observations on the Interaction of Poliovirus and Host Cells *in vitro*. III. The Effect of Some Bacterial Metabolites and Endotoxins.** *Brit. J. Exper. Path.* 1959, Aug., v. 40, No. 4, 391–7, 5 figs.

Dane *et al.* [this *Bulletin*, 1957, v. 32, 311] noted that some people without antibody failed to excrete poliovirus after taking attenuated poliovaccine by mouth. One explanation for this could be that the bacterial flora of the intestinal tract can inhibit multiplication of the virus. This possibility was investigated by culturing faeces from 3 persons (A, B and C) and preparing sterile filtrates of broth cultures of the mixed flora obtained on MacConkey, Leifson and blood agar plates. Endotoxins were prepared from 4 strains of *Escherichia coli*, 2 strains of *Streptococcus faecalis* and 1 diphtheroid derived from individual C by freezing and thawing. It was found that the yield of type 1 poliovirus (Mahoney) in monkey kidney cells was lowered after treatment with the crude filtrates although the results were only significant for individual C. The crude filtrate from individual C was effective in lowering the titre of poliovirus when diluted 1/100. 3 of the strains of *E. coli* isolated from C yielded endotoxin inhibiting the multiplication of poliovirus. A glucolipid polysaccharide endotoxin from *Salmonella typhimurium* was found to have an even more pronounced effect. A 1/10 dilution appeared to completely inhibit poliovirus production when given 3 days before virus and to have a profound effect even when given simultaneously. It did not, however, prevent or diminish the cytopathic effect of the poliovirus.

[For Parts I and II, see *ibid.*, 1959, v. 34, 398, 833.]
A. J. Beale

Rothstein, E. L. & Manson, L. A. **Phosphorus Incorporation into High Molecular Weight RNA of Poliovirus-Infected HeLa Cells.** [Correspondence.] *Virology.* New York. 1959, Sept., v. 9, No. 1, 141–3.

Mountain, Isabel M. & Alexander, Hattie E. **Infectivity of Ribonucleic Acid (RNA) from Type I Poliovirus in Embryonated Egg.** *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 527–32. [13 refs.]

Type 1 poliovirus (Mahoney strain) will not multiply in chick embryos. The RNA derived from poliovirus by the phenol extraction method of Gierer and Schramm (*Ztschr. f. Naturforsch.*, 1956, v. 11b, 138)

will produce plaques on susceptible cells but unlike intact virus is destroyed by ribonuclease. This poliovirus RNA yields fresh intact virus following inoculation into the amniotic cavity of 7–8-day developing chick embryos. The maximum yield of virus is 6–8 hours after infection. Treatment of the poliovirus RNA prevents multiplication. The virus yield is indistinguishable from intact virus; it is resistant to ribonuclease, is of type 1 and is unable to propagate in chick embryos. In preliminary work it was found that poliovirus RNA was not destroyed by amniotic fluid but was impaired by yolk sac and allantoic fluid. Similarly DNA from an *H. influenzae* transforming principle was unaffected by amniotic fluid.

[These results are similar to those reported by HOLLAND *et al.*, see this *Bulletin*, 1959, v. 34, 1193.]

A. J. Beale

ROIZMAN, B. **Preparation of High Potency Poliovirus in FL Cell Cultures at Room Temperature.** *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 410–11, 1 fig.

At 37°C. the peak intracellular titre of FL human amnion cells infected at high multiplicity with Mahoney type 1 poliovirus is reached at 10–12 hours, whereas the peak titre in the extracellular fluid occurs about 4 hours later. If virus adsorption took place at 37°C. and thereafter the cultures were held at 32°C. the peak titre in the cells was reached between 16–22 hours, but virus release was greatly delayed. Following this observation a series of bottle cultures of FL cells were infected at high multiplicity with poliovirus type 1 at 37°C. and then the fresh virus in the cells was harvested after 18–20 hours at room temperature (between 26 and 32°C.). At the time of harvest the supernatant fluid was discarded and the cells were scraped off the glass and packed by centrifugation at 1,000 r.p.m. These cells were stored at − 55°C. until they were disrupted with a Mickle Tissue Disintegrator. In this way very high yields of virus were obtained, of the order of 1×10^{10} plaque forming units per ml. and approximately 1,000 complement fixing units of D-antigen. From the amount of D-antigen it was calculated that there were about 10^{13} physical virus particles [this *Bulletin*, 1958, v. 33, 1094 *bis*].

A. J. Beale

BENYESH-MELNICK, Matilda & MELNICK, J. L. **Neutralizing-Antibody-Combining (NAC) Test for measuring Antigenic Potency of Poliomyelitis Vaccine.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1075–98, 3 figs. [11 refs.]

A neutralizing-antibody-combining (NAC) test for measuring the antigenic potency of poliovaccine is described. This work was initiated because of the irregularities noticed when the potency of poliovaccine is determined in animals. In this method 1 ml. of vaccine and 1 ml. of serum were held together at 37°C. for 6 hours and then 1 ml. of challenge virus was added and allowed to react for 6 hours. Finally the amount of residual infectious virus was determined by counting plaques. It was possible to store the mixtures at 4°C. overnight without influencing the results of the test. The important features of the test were found to be as follows: (1) The dose of virus; this was fixed at 1,000 plaque-forming units. (2) The dose of antiserum; the optimum dose was found to be that capable of neutralizing 99% of the virus. (3) The temperature and duration of incubation of the mixtures; it was found necessary to incubate for 6 hours at 37°C. to establish complete irreversible combination of antibody to poliovirus or poliovaccine. (4) The order of addition of vaccine and virus; it was important to allow vaccine and sera to react together first before challenge with live virus. The exact method of performing the test is described.

The neutralizing-antibody-combining power of vaccine was expressed as that dilution of vaccine which combines with 33% of the neutralizing antibody present in the serum. This 33% unit was found to be more sensitive than, and as accurate as, the 50% unit. It was found desirable to express the activity of a vaccine by its potency ratio to a standard vaccine preparation (Salk's vaccine J). The antigen-antibody union was found to be irreversible; the virus-antibody union could not be reversed by the subsequent addition of the vaccine as described by KRECH [this *Bulletin*, 1955, v. 30, 729]. The standard error of the ratio to vaccine J for different vaccines was usually less than 0·10 and the ratios to vaccine J remained stable in many repeat tests over a period of several months. The tests were equally satisfactory with monovalent vaccines or with trivalent vaccines. Similarly the test could be performed on vaccines stored with preservatives provided they were dialysed against Hanks solution before testing. The correlation between this test and the *in vivo* potency test with either chicks or monkeys was not very exact. This was thought to be explicable on the basis of the known great variations of the *in vivo* tests. In general it was found that vaccines with high potency ratios in the NAC test showed good potency in animals, but occasionally poor vaccines by the *in vitro* test gave quite reasonable results in the *in vivo* test. Freeze-dried poliovaccine retains its complement-fixing antigen titre undiminished, as described by HARE and WARREN [*ibid.*, 1959, v. 34, 505], but lacks *in vivo* potency. It also lacks the ability to combine with neutralizing antibody.

The authors suggest that this method of testing potency might prove very useful in assessing the life of poliovaccine and also in selecting monovalent pools for incorporation into final vaccine. They point out, however, that tests on the antibody response of triple negative children, correlated with the NAC test, are required before the method could be used to define the level of potency of vaccine. *A. J. Beale*

MELÉN, B. **Potency of Inactivated Poliovirus Vaccines. An *in vitro* Method for Assay for Antibody Combining Capacity.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 2, 135–49, 5 figs. [12 refs.]

The development of an *in vitro* antibody combining power test for the antigenicity of poliovirus preparations is described. Most of the work was done with

type 1 poliovirus and the inactivated preparations prepared from it, but the same method was applicable to type 2 and type 3 poliovirus. Antiserum, vaccine and challenge poliovirus were mixed together and after an appropriate interval the residual living virus was titrated in tissue culture tubes. Two-fold serial dilutions of the preparation under test in 2 ml. amounts were mixed with 0·25 ml. of the challenge virus preparation containing about 10,000 TCD50 per ml., and specific antiserum at a dilution which reduced the titre of virus (in the absence of antibody blocking) by 1 log unit. Since virus inactivated at 37°C. combined with antibody, the challenge virus was harvested as early as possible in the multiplication cycle in order to yield the highest proportion of living virus particles. The end-point was taken as that dilution of vaccine which reduced the power of the serum so that the challenge virus titre was 0·6 of a log unit below the titre obtained in a high parallel titration of the virus alone. It was found possible by this method to assess the antibody combining power of live virus as well as of inactivated preparations. The test gave very reproducible results having a standard deviation of 0·116 of a log unit.

The results of antigen extinction titrations in guinea-pigs, and of the antibody combining power test, indicated that the two methods were measuring the same property. There was no evidence of cross reactions between the 3 types of poliovirus in these tests. 3 preparations were tested at the beginning of formalin treatment and after the completion of formalin inactivation. There was very little difference between the antigen combining power of these two preparations, the fall was at the most 0·3 of a log unit. Over the range of virus antibody ratios used in this test the degree of inactivation of virus was inversely proportional to the amount present. However, when the amount of antiserum was increased, the proportion of virus neutralized seemed to be independent of the virus concentration, thus demonstrating the so-called percentage law [this *Bulletin*, 1934, v. 9, 279].

A. J. Beale

MELÉN, B. & SALENSTEDT, R. **Potency of Inactivated Poliovirus Vaccines. The Guinea Pig Test as a Routine Method.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 2, 150–55.

The antigenic potency of 22 Swedish poliovaccines and 23 imported vaccines (from the U.S.A., Canada and Europe) were tested by the antigen extinction method in guineapigs devised by GARD *et al.* [this *Bulletin*, 1956, v. 31, 757]. It was found that the vaccines varied markedly in their antigenic potency. In potency the type 2 and type 3 components appeared to be superior to the type 1, in particular some batches showed exceptionally high titres for type 3 (extinction limit greater than 10^{-3}). The potency of the Swedish vaccines in respect of the type 1 component appeared to be slightly superior to that of the imported vaccines. The standard deviation of the test was found to be 0·27 and 0·28 of a log unit when the results were corrected for that obtained with the standard living virus preparation.

One of the sources of error was found to be the method of performing the neutralization test. Originally 100 TCD of virus were mixed for 1 hour at room temperature with undiluted serum. The mixture was then inoculated into 2 tissue culture tubes. Later an improved method was used, involving serum diluted 1 to 5 mixed with 100 TCD50 of virus and held at 37°C. for 18 hours, which allowed complete neutralization to take place. The virus-serum mixture was then inoculated into 4 tubes. Neutralization was considered to have taken place if 2 of the tubes were protected from the action of the virus. Storage of the vaccine for 2 weeks to 8 months at 4°C. had very little effect upon the antigenic potency. In one experiment a vaccine that had been ampouled with only 50% of the formaldehyde neutralized lost potency after 7 months' storage at 4°C. by approximately 0·5 of a log unit for all 3 types of virus. Otherwise vaccine stored for at least 8 months at 4°C. did not appear to lose potency.

A. J. Beale

LÉPINE, P., ROGER, F. & ROGER, Annie. La réaction cinétique de séro-neutralisation des virus poliomyélitiques. [**The Kinetic Reaction for Measuring Serum Neutralizing Antibody against Poliovirus**] *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 4, 563–78. [14 refs.]

A new qualitative measure of serum neutralizing antibody against poliovirus is described. In this method virus (0·45 ml.) and serum (0·05 ml.) are allowed to react for 3 hours at 37°C. in Kahn tubes held vertically. 10^5 KB cells are then added in 0·25 ml. quantities and finally, after ½ hour at room temperature, the cultures are sealed with oil after the addition of more medium containing sufficient calf or chick serum to give a final concentration of 9%. They are incubated vertically at 37°C. and read for cytopathic effects with an inverted microscope at 48 and 72 hours. The challenge dose of virus is the least dilution that will destroy all the 6 to 8 tubes of cells at that dilution in 72 hours. The serum contains antibodies if the cells are protected at 3 days. The method is rapid and easy to perform. Accuracy depends upon a reproducible cell population and exact timing of reading the results. It has proved extremely economical for epidemiological and survey work. Full practical details are given. *A. J. Beale*

LEDINKO, Nada. **Blocking of Neutralizing Antibody by Noninfective Poliovirus from Proflavine-Treated HeLa Cells.** [Correspondence.] *Virology.* New York. 1959, Aug., v. 8, No. 4, 536–9, 1 fig.

The author has previously reported that when HeLa cells are infected with poliovirus in the presence of proflavine (2·5 μgm.-ml.) the cells are destroyed but no infectious virus is released. The yield of complement-fixing antigen and virus particles determined by electron microscopy [LEDINKO, this *Bulletin*, 1959, v. 34, 294] is similar to that following infection of untreated cells. It is now shown that such non-infectious virus is capable

of combining with neutralizing antibody to the same degree as virus inactivated by ultraviolet rays, and thus blocking the power of antiserum to neutralize living virus. These tests were done with Brunhilde type 1 poliovirus. *A. J. Beale*

MORGAN, C., HOWE, C. & ROSE, H. M. **Intracellular Crystals of Coxsackie Virus viewed in the Electron Microscope.** [Correspondence.] *Virology.* New York. 1959, Sept., v. 9, No. 1, 145–9, 3 figs. [11 refs.]

GODTFREDSEN, Annelise. **Strains of Coxsackie Virus Type A–9 and ECHO Virus Type 9 recovered from Cerebrospinal Fluids.** *Acta Path. et Microb. Scandinavica.* 1959, v. 46, No. 3, 217–22. [18 refs.]

"During 1957 cerebrospinal fluids from a total of 306 patients were examined in monkey kidney tissue cultures. Most of these patients presented symptoms from the central nervous system. Echo virus type 9 was isolated from 21 cerebrospinal fluids and Coxsackie virus type A-9 from 2 cerebrospinal fluids. Two of the cytopathogenic agents could not be identified as poliovirus or echovirus types 1–14. These two strains were not pathogenic for newborn mice.

"The two cerebrospinal fluids from which Coxsackie virus type A-9 was isolated in tissue culture did not induce paralysis in newborn mice by primary inoculation.

"Serological studies on paired sera from 18 patients harbouring echovirus type 9 in the spinal fluid revealed an increase in neutralizing antibody titer in 13 instances. In 5 cases no significant rise in titer could be demonstrated.

"Neutralization tests on paired sera from the 2 patients harbouring Coxsackie virus type A-9 in the cerebrospinal fluid showed in both cases an increase in titer against Coxsackie virus type A-9."

MCINTOSH, E. G. S. & SOMMERVILLE, R. G. **An Analysis of 24 Strains of ECHO Virus Type 7.** *Arch f.d. gesamte Virusforschung.* 1959, v. 9, No. 2, 261–6.

24 strains of ECHO virus type 7 isolated in Glasgow were compared with the prototype Wallace strain of ECHO type 7. With antiserum prepared against the prototype virus no significant antigenic differences were detected between the ECHO 7 strains. Similarly all the isolates produced plaques of the same size and appearance at the same time on monkey kidney cells and all the strains were non-pathogenic for suckling mice less than 24 hours old. The strains differed, however, in their ability to haemagglutinate 1% washed human group O red cells. The prototype strain agglutinates these cells at 37°C. and at 4°C. Only 8 of the Glasgow strains produced haemagglutinin and the titre varied markedly from strain to strain and did not appear to be correlated with the infectivity titre for monkey kidney cells.

The possibility that the haemagglutinin observed was due to a contaminating simian virus was considered since HULL *et al.* [this *Bulletin*, 1956, v. 31, 873] have shown that many of the simian viruses cause agglutination of human red cells. All the virus pools used for the haemagglutination test were prepared in the same batch of monkey kidney cells. Trouble with spontaneous degeneration of monkey kidney cells which could be due to simian viruses has not been noted by the authors. Therefore a contaminating simian virus did not appear to be the cause of the haemagglutination. *A. J. Beale*

PHILIPSON, L. **Studies on the Mechanism of Haemagglutination by Echo-Viruses. I. Evidence for Enzymatic Degradation by Chymotrypsin of the Receptor for Echo-Viruses.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 2, 251–60, 3 figs. [15 refs.]

It has been found that the treatment of human group O red cells with chymotrypsin renders them inagglutinable by ECHO viruses (the prototype strains of ECHO 7, 11, 18, 19, 20, 22 and 23 as monkeys kidney tissue culture fluids were used). Other enzymes, trypsin, elastase, carboxypeptidase, phospholipase A and C, were without effect. The absence of any effect with elastase is interesting as this enzyme and chymotrypsin are identical on amino acid substrates. The action of chymotrypsin was on some specific receptor for ECHO viruses on the red cells. Treated cells were still agglutinable by myxoviruses, but neither the infective particle nor the haemagglutinin of ECHO viruses was adsorbed to such treated cells. The elution of virus that did adsorb to partially treated cells was not affected by chymotrypsin treatment. *A. J. Beale*

LAHELLE, O, with the technical assistance of A. MAURSETH. **Inhibition of the ECHO Virus Haemagglutination by Specific ECHO Antisera.** *Acta Path. et. Microb. Scandinavica.* 1958, v. 44, No. 4, 413–20.

"The ECHO virus 6 strain La and the prototype strains 3, 7, 11, 13 and 19, propagated in human amnion cell cultures agglutinate human erythrocytes. The hemagglutinations are dependent upon the temperature. The type 7 strain causes maximal agglutination at 4°C and 37°C. The type 6 strain shows maximal titer at 37°C. while the other type strains have maximal titers at 4°C.

"The hemagglutinations are inhibited by ECHO antisera prepared in rabbits. The inhibition reactions are carried out at 4°C with sera adsorbed with human red cells. The ECHO type strains are neutralized by homologous but not by heterologous antisera. The hemagglutination inhibition test is less specific. The ECHO 7 hemagglutinin is inhibited only by the homologous antiserum, but the other type hemagglutinins are inhibited also by certain heterologous antisera."

SABIN, A. B. **Survey of Knowledge and Problems in Field of Arthropod-Borne Virus Infections.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 1, 1–10, 1 fig. [26 refs.]

74 distinct aborviruses have so far been recognized but 50 of them are still "in search of a disease". Antibodies have been found in man to 14 of these 50 viruses. Because of its intermediate tissue tropism and because of some serological evidence, West Nile virus may be the most primitive existing form in Casal's Group B of arborviruses. The geographical distribution of the Group B viruses is discussed in this light: in Africa the evolutionary trend seems to have been towards viscerotropism, compared with a greater tendency to neurotropism elsewhere. The significance of cross immunity between related arborviruses is discussed but this is not considered of ecological importance. The problem of vaccine control is outlined, and the possible use of the broader serological responses following a killed vaccine, when it has been preceded by an infection with an avirulent related virus, is mentioned.

C. E. Gordon Smith

SCHMIDT, J. R., GAJDUSEK, D. C., SCHAEFFER, M. & GORRIE, Rachel H. **Epidemic Jungle Fever among Okinawan Colonists in the Bolivian Rain Forest. II. Isolation and Characterization of Uruma Virus, a Newly Recognized Human Pathogen.** *Amer. J. Trop. Med. & Hyg.* 1959, July, v. 8, No. 4, 479–87.

Blood was collected from 3 febrile patients during an epidemic in the Uruma colony in Bolivia. A virus was isolated by intracerebral inoculation of 1-day-old mice with fluid from a culture of MB III cells inoculated at Uruma. The virus was subsequently isolated also from the frozen blood of the same patient and from similar blood of another patient. Filtration and ultracentrifugation suggested that the size of the virus was 17–26 mμ. 1-day-old mice were highly susceptible to intracerebral or intraperitoneal inoculation with a minimum incubation period of 2–4 days. Mice 3–4 days old were less susceptible and 10-day mice insusceptible. Inoculated guineapigs showed only a febrile reaction and rabbits none. Newborn hamsters were highly susceptible, but not adults. Yolk-sac inoculation of chick embryos caused death of the embryos at the 7th egg passage in an average of 3·6 days. Cytopathic effects were caused in tissue cultures of hamster kidney, KB, human liver and monkey kidney cells, but not in HeLa, human conjunctiva, or MB III cells.

The virus was compared in neutralization tests with antisera to 32 neurotropic viruses and a relationship found only to Semliki Forest and Sindbis viruses. It was also compared with H290 virus isolated at Belem, Brazil, and a close relationship found. H290 is closely related to Mayaro virus [this *Bulletin*, 1958, v. 58, 536]. Uruma virus was found to haemagglutinate at 4°, 22° and 37°C. at an optimum *p*H of 6·4 to 6·6. Haemagglutinin-inhibition tests revealed a relationship in decreasing order with Mayaro, Semliki Forest, western equine, Sindbis and eastern equine viruses. Complement-fixation tests showed similar relationships when antigen dilutions were tested against constant amounts of antiserum, but differences were much more marked when serum dilutions were tested against constant amounts of antigen. Serial serum specimens from the patient from whom the virus came showed a highly significant rise in antibody level confirming the origin of the virus. Convalescent sera from 3 of 38 other patients from the Uruma outbreak had neutralizing antibody as did 8 of 21 people from a settlement 21 km. away.

[For Part I, see *ibid.*, 1959, v. 35, 1234.]

C. E. Gordon Smith

SELIGMAN, S. J. & RAPP, F. **A Variant of Measles Virus in which Giant Cell Formation appears to be genetically determined.** [Correspondence.] *Virology.* New York. 1959, Sept, v. 9, No. 1, 143–5.

CONGIU, S. & SOBRERO, L. Virus fisso della rabbia in Somalia. [**Fixed Rabies Virus in Somalia**] *Ann. Soc. Med. Igiene Trop. Somalia.* 1954–8, v. 2, 113–25.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 28.]

IMMUNITY

TURK, J. L. **The Relationship between Complement and Antibodies of Different Animals in the Immune-Adherence Phenomenon.** *Immunology.* Oxford. 1959, Apr., v. 2, No. 2, 127–36. [14 refs.]

"Normal adult spleen cells were antigenically stimulated by incubation with isolated flagella from *Salmonella* bacteria, and after neutralization of free antigen and washing, were transferred to normal and sublethally X-irradiated mice and rats of various ages by intraperitoneal injection. Neonatal rats and Hall Institute mice could not produce antibody following such injections, but more mature rats and Hall Institute mice, and neonatal C_3H mice, could produce antibody.

"Cells from immunized spleens were secondarily stimulated *in vitro* and transferred to neonatal and more mature recipients. Regardless of the age of the recipients, antibody production typical of a secondary response ensued.

"Cells from neonatal rat spleens were stimulated *in vitro* and transferred to more mature recipient rats. Some antibody production resulted.

"The theoretical implications of these findings are discussed."

NOSSAL, G. J. V. **Studies on the Transfer of Antibody Producing Capacity. I. The Transfer of Antibody Producing Cells to Young Animals.** *Immunology.* Oxford. 1959, Apr., v. 2, No. 2, 137–47, 6 figs. [12 refs.]

"A comparison is made of the titres of complement from different animals when reacting with antisera from different species, in the immune-adherence phenomenon. A failure of reaction between rabbit antibody and horse and pig complement is noted. This may be overcome by the addition of heated guineapig serum. Whereas a similar failure of reaction between rabbit antibody and horse complement in immune haemolysis is also overcome by the addition of ammonia-treated guinea pig serum, this does not occur in immune-adherence. This is interpreted as meaning that there is a further heat-stable ammonia-sensitive co-factor necessary for immune-adherence in addition to the four components of complement. This co-factor is also inactivated by zymosan.

"The behaviour of mouse complement in immune-adherence indicates a relative deficiency in C'2 as in immune haemolysis.

"Conglutinin is shown to inhibit immune-adherence irrespective of the species of complement used."

Book Review

GEAR, Harry Sutherland [M.D., D.P.H., D.T.M. & H., B.Sc., F.S.S.]. **World Medical Research. Principles and Practices.** pp. xii+117+[5]. 1959. London: Butterworth and Co. (Publishers) Ltd., 88, Kingsway, W.C.2 [30s.]

In recent years interest in international research has increased greatly, a strikingly successful example being the International Geophysical Year. International medical research has begun to attract interest and in 1958 the United Nations invited the World Health Organization to consider the organization of an International Health and Medical Research Year. The book reviewed here gives a brief account of the functioning of research under the authority of the World Health Organization and other bodies established by the United Nations. Since medical art and science developed in many lands and cultures it is appropriate that the review should start with a brief history of medicine from its earliest beginnings. It is interesting to note how research was actively pursued during certain periods, and how it became officially sponsored by governments in the 19th and 20th centuries.

Research was accepted as one of the functions of the World Health Organization at its inception and it was decided that in the first place it should be connected with current programmes and should be supported in existing institutions. In only one instance, the European Organization for Nuclear Research, has a laboratory been specifically operated as an international research laboratory. In other cases research has been undertaken at the request of member states in their own official and non-official laboratories. Assistance is given to them through fellowships, appointment of teaching staff, advice from advisory panels and in a host of other ways. Subjects for research are indicated, techniques taught and methods standardized. Most of the research has been connected with communicable disease, but applied research has disclosed problems requiring fundamental research. Programmes in political and economic fields have a considerable influence on health and so many of the organizations under the United Nations are concerned directly or indirectly with research concerning health, and these have led to a variety of forms of international co-operation in research.

Some interesting issues are raised. Under the stress of poverty and population pressure the under-developed countries are being driven to train technologists for industrialization at the expense of other educated groups, but ultimately the vigour of science and technology is dependent on the existence of independent individuals with a love for a full life of culture and thought. A problem created by expanding international research is the withdrawal from productive work of scientists needed for full-time administration or consultative work. Other difficulties connected with international research are raised and discussed. Finally the author considers the future of international medical research and makes some suggestions for improving and expanding it. He advocates the establishment and encouragement of universities in which a suitable climate for research will be provided; this would necessitate the prior provision of moral and material aid to education generally. Biology, in particular, needs support because in competition with industrial technology it attracts few students, but it is essential for medical and related sciences.

In view of the increasing attention devoted to international medical research the publication of this book is to be welcomed. It depicts contemporary arrangements in this field and discusses the activities, prob'ems, organization and difficulties connected with it. The book will, therefore, be of value to all who are interested in this developing field of work, and particularly to those associated with its activities.

T. H. Davey

Printed in Great Britain by The Eastern Press, Ltd., London and Reading